Supplementary data for the article:

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Supporting Information

Enantioselective Synthesis of the Platensimycin Core by Silver(I)-Promoted Cyclization of Δ^6-α-Iodoketone

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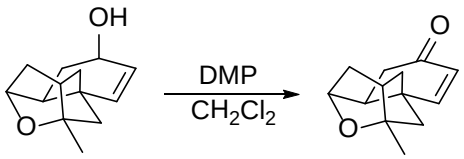
Contents

General experimental

All chromatographic separations[1] were performed on silica gel, 10–18 mesh, 60 Å (dry flash) and silica gel 60 (0.063-0.2 mm), Merck. Standard techniques were used for the purification of the reagents and solvents.[2] Petroleum ether refers to the fraction boiling at 70–72 °C. NMR spectra were recorded with a Bruker Avance III 500 (^{1}H NMR at 500 MHz, ^{13}C NMR at 125 MHz). Chemical shifts are expressed in ppm (δ) using tetramethylsilane as the internal standard, coupling constants (*J*) are in Hz. IR spectra were recorded with a Nicolet 6700 FT instrument and expressed in cm^{-1}. Mass spectra were obtained with an Agilent Technologies 6210 TOF LC– MS instrument (LC: series 1200) and LTQ Orbitrap XL hybrid FTMS (Thermo Scientific). Melting points were determined with Electrothermal apparatus and are uncorrected. Optical rotation was determined with a Rudolph Research Analytical AUTOPOL IV Automatic Polarimeter.

Experimental procedures in numerical order

(4a*S*,5*S*,8*S*,9a*S*)-8-Methyl-4a,5,6,7,8,9-hexahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-3(4*H*)-one (1)

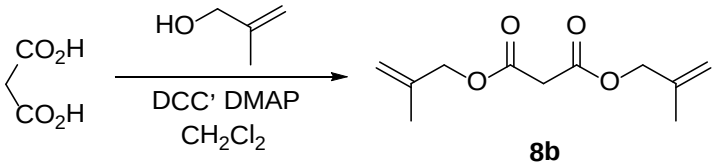


41 **1**

To a solution of alcohol **41** (3.6 mg; 0.017 mmol) in dichloromethane (1.0 mL) was added Dess-Martin periodinane (10.8 mg; 0.025 mmol; 1.5 eq.) and the reaction mixture was stirred for 15 min at room temperature. The reaction mixture was washed with 10% $Na_2S_2O_{3\,(aq)}$ and sat. $NaHCO_{3\,(aq)}$, the organic layer was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 1:1), to afford 2.8 mg (80%) of the titled compound **1**, as a colorless oil (spectroscopic data in agreement with the literature).[3]

R_f = 0.47 (SiO_2, petroleum ether/ethyl acetate = 1:1).
[α]$_D^{20}$ –21.5 (*c* 0.26, $CHCl_3$); literature value[3] -21.0 (*c* 0.50, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (d, *J* = 10.0 Hz, 1H), 5.94 (d, *J* = 10.0 Hz, 1H), 4.16 (t, *J* = 3.8 Hz, 1H), 2.43 – 2.38 (m, 1H), 2.36 – 2.26 (m, 3H), 1.98 – 1.92 (m, 2H), 1.89 (d, *J* = 11.6 Hz, 1H), 1.78 – 1.72 (m, 2H), 1.66 (d, *J* = 11.2 Hz, 1H), 1.44 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.0 (C), 155.1 (CH), 128.9 (CH), 87.0 (C), 79.0 (CH), 51.7 (CH_2), 46.2 (C), 44.2 (CH), 42.7 (CH), 42.2 (CH_2), 37.9 (CH_2), 37.5 (CH_2), 23.1 (CH_3).

***bis*(2-Methylallyl) malonate (8b)**



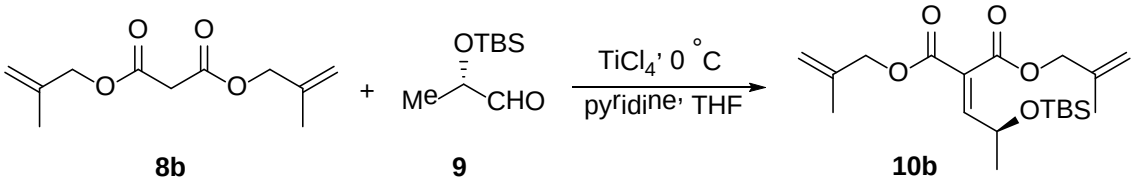
8b

To a solution of malonic acid (6.24 g; 59.97 mmol) and β-methallyl alcohol (8.67 g; 120.23 mmol; 2 eq.) in dichloromethane (200 mL) were added DCC (26.00 g; 126.01

mmol; 2.1 eq.) and DMAP (0.73 g; 5.97 mmol; 10 mol%). The reaction mixture was stirred for 3 h at room temperature, then filtered under reduced pressure and the precipitate was washed three times with ethyl acetate. The filtrate was concentrated on rotovap and the residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5), to afford 10.79 g (85%) of diester **8b**, as a colorless oil.

R_f = 0.25 (SiO_2, petroleum ether/ethyl acetate = 95:5).
^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.01 – 4.99 (m, 2H), 4.96 – 4.94 (m, 2H), 4.58 (s, 4H), 3.46 (s, 2H), 1.76 (s, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ: 166.1 (2xC), 1s39.3 (2xC), 113.6 (2xCH_2), 68.7 (2xCH_2), 41.5 (CH_2), 19.4 (2xCH_3).
IR (ATR) *v* 3084, 2979, 2946, 1740, 1659, 1451, 1331, 1270, 1149, 1006, 907 cm^{-1}.
HRMS (ESI) calculated for $C_{11}H_{17}O_4^+$ $[M+H]^+$: 213.1121, found: 213.1129.

(*S*)-*bis*(2-Methylallyl) 2-(2-((*tert*-butyldimethylsilyl)oxy)propylidene)malonate (10b)

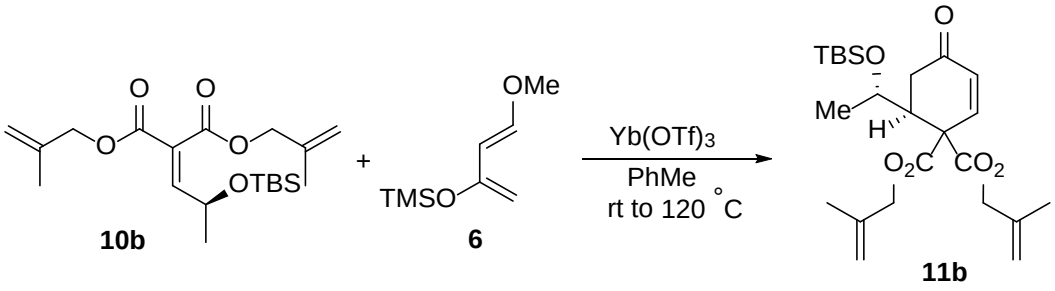


8b **9** **10b**

A solution of diester **8b** (4.24 g; 19.98 mmol) and aldehyde[4] **9** (4.35 g; 23.10 mmol; 1.16 eq.) in THF (45 mL) was added to a suspension of titanium(IV) chloride (8.65 g; 5.0 mL; 45.60 mmol; 2.3 eq.) in THF (110 mL), at 0 °C and under an argon atmosphere. After 10 min of stirring at 0 °C (the yellow reaction mixture turns brick red), pyridine (7.34 g; 7.5 mL; 92.73 mmol; 4.64 eq.) was added and the mixture was stirred for 10 min at 0 °C and then for additional 36 h at room temperature. The reaction was quenched by a careful addition of sat. $NH_4Cl_{(aq)}$ and mixture was extracted with diethyl ether (3 x 450 mL). The organic extract was washed with brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 975:25), to afford 7.35 g (96%) of the titled compound **10b**, as a colorless oil.

R_f = 0.42 (SiO_2, petroleum ether/ethyl acetate = 95:5).
[α]$_D^{20}$ +13.2 (*c* 1.20, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 6.96 (d, *J* = 8.1 Hz, 1H), 5.06 – 4.94 (m, 4H), 4.76 – 4.69 (m, 1H), 4.68 (d, *J* = 13.4 Hz, 1H), 4.63 – 4.58 (m, 3H), 1.79 (s, 3H), 1.76 (s, 3H), 1.30 (d, *J* = 6.4 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 164.5 (C), 163.5 (C), 153.2 (CH), 139.4 (C), 139.2 (C), 125.3 (C), 114.1 (CH_2), 113.2 (CH_2), 68.8 (CH_2), 68.6 (CH_2), 66.2 (CH), 25.8 (3xCH_3), 23.4 (CH_3), 19.6 (CH_3), 19.4 (CH_3), 18.1 (C), -4.7 (CH_3), -5.0 (CH_3).
IR (ATR) *ν* 3083, 2954, 2932, 2859, 1732, 1657, 1453, 1369, 1253, 1205, 1111, 1088, 907, 835, 778 cm^{-1}.
HRMS (ESI) calculated for $C_{20}H_{35}O_5Si^+$ $[M+H]^+$: 383.2248, found: 383.2236.

bis(2-Methylallyl) 6-((*S*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl)-4-oxocyclohex-2-ene-1,1-dicarboxylate (11b)

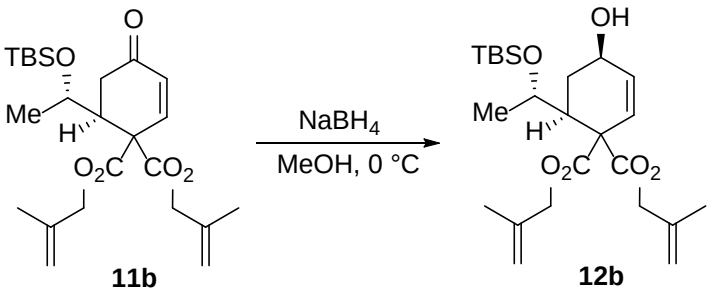


Ytterbium(III) triflate hydrate (38.4 mg; 0.06 mmol; 1 mol%) was added to a solution of Danishefsky diene **6** (1.39 g; 8.07 mmol; 1.38 eq.) and malonate **10b** (2.24 g; 5.86 mmol) in toluene (35 mL), at rt and under an argon atmosphere. The reaction mixture was stirred for 10 min at room temperature (at this point, the acyclic Mukaiyama intermediate could be isolated) and than for additional 1 h at 120 °C. The reaction was quenched with water and the mixture was extracted with dichloromethane (3 x 150 mL). The combined organic extract was dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5), to afford 2.58 g (98%) of the titled compound **11b**, as a colorless oil.

R_f = 0.50 (SiO_2, petroleum ether/ethyl acetate = 85:15).
[α]$_D^{20}$ +130.6 (*c* 1.14, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.01 (dd, J = 10.3, 1.5 Hz, 1H), 6.04 (dd, J = 10.3, 0.8 Hz, 1H), 5.01 – 4.94 (m, 2H), 4.93 – 4.89 (m, 2H), 4.65 (d, J = 12.7 Hz, 1H), 4.58 – 4.48 (m, 3H), 3.90 (qd, J = 6.2, 1.0 Hz, 1H), 2.97 – 2.93 (m, 1H), 2.84 (dd, J = 17.3, 6.1 Hz, 1H), 2.69 (dd, J = 17.3, 2.3 Hz, 1H), 1.73 (s, 3H), 1.68 (s, 3H), 1.17 (d, J = 6.3 Hz, 3H), 0.77 (s, 9H), -0.05 (s, 3H), -0.06 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ: 196.7 (C), 168.1 (C), 167.4 (C), 141.3 (CH), 138.8 (C), 138.7 (C), 131.0 (CH), 114.6 (CH_2), 113.9 (CH_2), 69.4 (CH_2), 69.2 (CH_2), 68.9 (CH), 58.6 (C), 46.0 (CH), 34.4 (CH_2), 25.7 (3xCH_3), 23.4 (CH_3), 19.5 (CH_3), 19.3 (CH_3), 17.9 (C), -4.5 (CH_3), -4.6 (CH_3).
IR (ATR) ν 2931, 2892, 2857, 1740, 1694, 1457, 1382, 1255, 1226, 1185, 1144, 1075, 957, 839, 777 cm^{-1}.
HRMS (ESI) calculated for $C_{24}H_{39}O_6Si^+$ $[M+H]^+$: 451.2510, found: 451.2505.

bis(2-Methylallyl) (4*R*,6*S*)-6-((*S*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl)-4-hydroxycyclohex-2-ene-1,1-dicarboxylate (12b)



11b **12b**

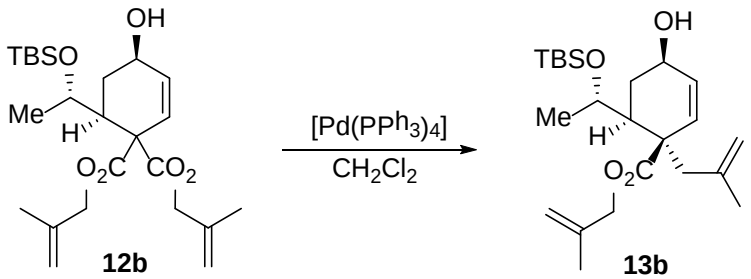
To a cold (0 °C) solution of enone **11b** (8.55 g; 18.97 mmol; 1.13 eq.) in methanol (150 mL), sodium borhydride (0.81 g; 21.41 mmol; 1.1 eq.) was added. The reaction mixture was stirred at 0 °C for 30 min, then methanol was evaporated under reduced pressure, and the residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 85:15), to afford 7.81 g (91%) of alcohol **12b**, as a colorless oil and 0.40 g (5%) of the diastereomeric alcohol, also in a form of a as colorless oil (*dr* = 19:1).

Spectral data for the major stereoisomer

$\boldsymbol{R_f}$ = 0.33 (SiO_2, petroleum ether/ethyl acetate = 85:15).
$[\alpha]_D^{20}$ +143.9 (*c* 1.08, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.12 (dt, J = 10.2, 1.1 Hz, 1H), 5.95 (ddd, J = 10.2, 4.1, 1.1 Hz, 1H), 5.03 – 4.86 (m, 4H), 4.57 (bs, 2H), 4.52 (d, J = 13.0 Hz, 1H), 4.46 (d, J =

13.0 Hz, 1H), 4.31 (d, *J* = 11.3 Hz, 1H), 4.06 (qd, *J* = 6.3, 2.2 Hz, 1H), 4.01 – 3.95 (m, 1H), 2.64 – 2.60 (m, 1H), 2.35 (dt, *J* = 15.5, 5.6 Hz, 1H), 2.17 – 2.11 (m, 1H), 1.73 (s, 3H), 1.69 (s, 3H), 1.31 (d, *J* = 6.3 Hz, 3H), 0.87 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9 (C), 168.9 (C), 139.2 (C), 139.0 (C), 131.9 (CH), 125.0 (CH), 113.9 (CH_2), 113.3 (CH_2), 69.2 (CH), 68.8 (CH_2), 68.7 (CH_2), 61.5 (CH), 57.6 (C), 41.3 (CH), 27.2 (CH_2), 26.0 (3xCH_3), 23.2 (CH_3), 19.4 (CH_3), 19.3 (CH_3), 18.2 (C), -4.5 (CH_3), -4.8 (CH_3).
IR (ATR) *ν* 3431, 3083, 2933, 2858, 1738, 1657, 1453, 1377, 1254, 1181, 1054, 943, 835, 780 cm^{-1}.
HRMS (ESI) calculated for $C_{24}H_{40}O_6SiNa^+$ $[M+Na]^+$: 475.2486, found: 475.2484.

2-Methylallyl (1*R*,4*R*,6*S*)-6-((*S*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl)-4-hydroxy-1-(2-methylallyl)cyclohex-2-ene-1-carboxylate (13b)



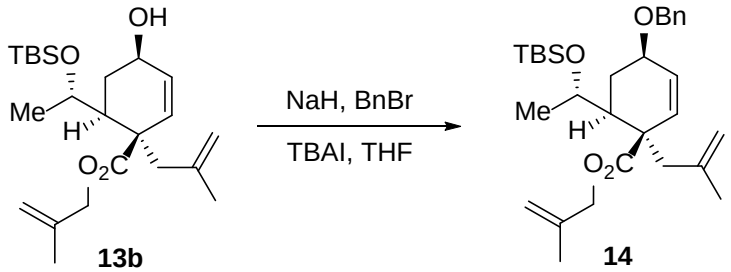
12b **13b**

Tetrakis(triphenylphosphine)paladium(0) (301.9 mg; 0.26 mmol; 1.6 mol%) was added to a solution of diester **12b** (7.54 g; 16.66 mmol) in dichloromethane (170 mL), under an argon atmosphere. The reaction mixture was stirred at room temperature for 1.5 h, and dichloromethane was evaporated under reduced pressure. The residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 9:1), to afford 6.68 g (98%) of the titled compound **13b**, as a colorless oil.

***R*$_f$** = 0.40 (SiO_2, petroleum ether/ethyl acetate = 85:15).
[α]$_D^{20}$ +108.2 (*c* 1.14, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.14 (dt, *J* = 10.4, 1.2 Hz, 1H), 5.78 (ddd, *J* = 10.4, 4.0, 1.2 Hz, 1H), 5.03 (bs, 1H), 4.97 (bs, 1H), 4.82 – 4.79 (m, 1H), 4.65 (bs, 1H), 4.61 (d, *J* = 13.1 Hz, 1H), 4.39 (d, *J* = 13.0 Hz, 1H), 4.29 (d, *J* = 11.2 Hz, 1H), 4.19 (qd, *J* = 6.4, 2.0 Hz, 1H), 4.03 – 3.98 (m, 1H), 2.56 (d, *J* = 12.7 Hz, 1H), 2.44 (d, *J* = 12.8 Hz, 1H), 2.25 (dt, *J* = 15.4, 5.6 Hz, 1H), 2.18 – 2.12 (m, 1H), 1.92 – 1.88 (m, 1H), 1.79 (s, 3H), 1.68 (s, 3H), 1.26 (d, *J* = 6.4 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4 (C), 141.5 (C), 139.4 (C), 130.5 (CH), 128.7 (CH), 115.2 (CH_2), 113.7 (CH_2), 69.2 (CH), 68.0 (CH_2), 61.9 (CH), 50.3 (C), 50.0 (CH_2), 45.3 (CH), 26.5 (CH_2), 26.0 (3xCH_3), 24.0 (CH_3), 23.4 (CH_3), 19.8 (CH_3), 18.1 (C), -4.4 (CH_3), -4.7 (CH_3).
IR (ATR) *ν* 3433, 3078, 2954, 2932, 2858, 1729, 1654, 1451, 1374, 1254, 1177, 1064, 962, 899, 835, 778 cm^{-1}.
HRMS (ESI) calculated for $C_{23}H_{41}O_4Si^+$ $[M+H]^+$: 409.2769, found: 409.2762.

2-Methylallyl (1*R*,4*R*,6*S*)-4-(benzyloxy)-6-((*S*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl) -1-(2-methylallyl)cyclohex-2-ene-1-carboxylate (14)



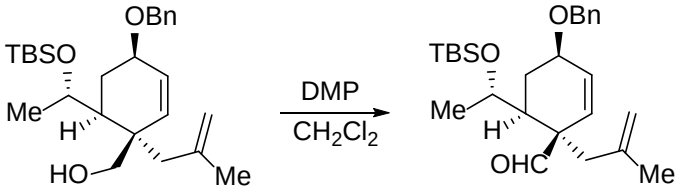
13b **14**

To a solution of alcohol **13b** (5.42 g; 13.26 mmol) in THF (27 mL) were added benzyl bromide (6.97 g; 4.85 mL; 40.78 mmol; 3 eq.), TBAI (0.52 g; 1.50 mmol; 11 mol%) and sodium hydride (0.95 g; 39.67 mmol; 3 eq.), under an argon atmosphere. The reaction mixture was stirred at room temperature for 24 h., then cooled to 0 ^oC and the reaction was quenched by a dropwise addition of acetic acid (3.5 mL). The reaction mixture was dilluted with ethyl acetate (200 mL) and washed with sat. $NaHCO_{3\,(aq)}$. The aqueous layer was extracted with ethyl acetate (2 x 200 mL), and the combined organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was dried under high vacuum to remove the excess of benzyl bromide and then purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 99:1), to afford 6.06 g (92%) of benzyl ether **14**, as a colorless oil.

$\boldsymbol{R_f}$ = 0.77 (SiO_2, petroleum ether/ethyl acetate = 95:5).
$\boldsymbol{[\alpha]_D^{20}}$ –70.7 (*c* 1.10, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 4H), 7.28 – 7.23 (m, 1H), 5.90 (dt, *J* = 10.3, 1.6 Hz, 1H), 5.63 (dd, *J* = 10.2, 2.1 Hz, 1H), 5.01 – 4.96 (m, 1H), 4.89 – 4.86 (m, 1H), 4.85 – 4.83 (m, 1H), 4.67 (s, 1H), 4.65 – 4.54 (m, 3H), 4.36 (d, *J* = 13.4 Hz, 1H), 4.26 (qd, *J* = 6.4, 2.6 Hz, 1H), 4.09 (ddt, *J* = 10.0, 5.8, 2.0 Hz, 1H), 2.62 (d, *J* = 14.1 Hz,

1H), 2.52 (d, *J* = 14.0 Hz, 1H), 2.14 (ddt, *J* = 12.8, 5.8, 2.0 Hz, 1H), 1.87 (td, *J* = 12.9, 10.3 Hz, 1H), 1.73 (s, 3H), 1.69 – 1.63 (m, 4H), 1.18 (d, *J* = 6.2 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) *δ* 173.0 (C), 142.2 (C), 139.8 (C), 139.1 (C), 132.4 (CH), 130.5 (CH), 128.3 (2xCH), 127.5 (2xCH), 127.4 (CH), 115.9 (CH_2), 112.7 (CH_2), 75.2 (CH), 69.4 (CH_2), 68.1 (CH_2), 66.6 (CH), 49.5 (C), 47.6 (CH), 45.1 (CH_2), 26.3 (CH_2), 26.1 (3xCH_3), 24.5 (CH_3), 24.2 (CH_3), 19.6 (CH_3), 18.3 (C), -3.5 (CH_3), -3.9 (CH_3).
IR (ATR) *ν* 3367, 3072, 3030, 2954, 2931, 2889, 2856, 1727, 1656, 1455, 1373, 1254, 1203, 1174, 1140, 1093, 1074, 1029, 1002, 944, 899, 834, 777, 737.
HRMS (ESI) calculated for $C_{30}H_{47}O_4Si^+$ $[M+H]^+$: 499.3238, found: 499.3228.

(1*R*,4*R*,6*S*)-4-(Benzyloxy)-6-((*S*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl)-1-(2-methylallyl)cyclohex-2-ene-1-carbaldehyde (15)



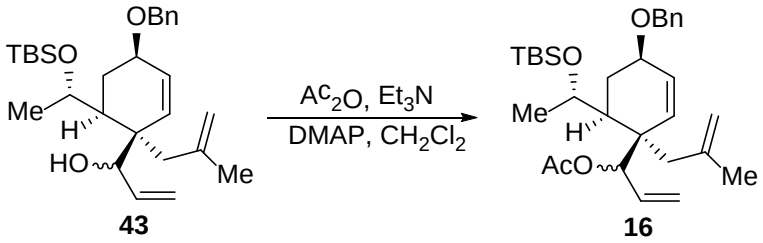
42 **15**

Dess-Martin periodinane (5.18 g; 12.21 mmol; 1.4 eq.) was added to a solution of alcohol **42** (3.79 g; 8.80 mmol) in dichloromethane (176 mL) and the reaction mixture was stirred for 30 min at room temperature. The reaction mixture was washed with 10% $Na_2S_2O_{3\,(aq)}$ and sat. $NaHCO_{3\,(aq)}$, the organic layer was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 975:25), to afford 3.69 g (98%) of aldehyde **15**, as a colorless oil.

***R*$_f$** = 0.38 (SiO_2, petroleum ether/ethyl acetate = 95:5).
[*α*]$_D^{20}$ –288.2 (*c* 1.02, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) *δ* 9.72 (s, 1H), 7.46 – 7.27 (m, 5H), 6.15 (dt, *J* = 10.1, 1.7 Hz, 1H), 5.25 (dd, *J* = 10.1, 2.1 Hz, 1H), 4.86 – 4.82 (m, 1H), 4.70 – 4.63 (m, 3H), 4.23 (dd, *J* = 13.7, 6.6 Hz, 1H), 4.17 (ddt, *J* = 10.0, 5.8, 1.9 Hz, 1H), 2.57 (d, *J* = 14.6 Hz, 1H), 2.42 (d, *J* = 14.5 Hz, 1H), 2.23 – 2.15 (m, 1H), 2.01 (dt, *J* = 13.4, 10.2 Hz, 1H), 1.85 – 1.78 (m, 1H), 1.67 (d, *J* = 1.3 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) *δ* 199.4 (CH), 142.4 (C), 138.5 (C), 134.2 (CH), 130.2 (CH), 128.5 (2xCH), 127.7 (2xCH), 127.7 (CH), 115.4 (CH_2), 74.9 (CH), 70.3 (CH_2),

66.2 (CH), 54.1 (C), 45.8 (CH), 40.1 (CH_2), 26.1 (3xCH_3), 24.4 (CH_2), 24.2 (CH_3), 22.1 (CH_3), 18.2 (C), -3.2 (CH_3), -4.6 (CH_3).
IR (ATR) *v* 3069, 3029, 2954, 2931, 2888, 2857, 2736, 1716, 1644, 1458, 1371, 1256, 1137, 1074, 1053, 1027, 945, 891, 834, 778, 738 cm^{-1}.
HRMS (ESI) calculated for $C_{26}H_{40}O_3SiNa^+$ $[M+Na]^+$: 451.2639, found: 451.2624.

1-((1*R*,4*R*,6*S*)-4-(Benzyloxy)-6-((*S*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl)-1-(2-methylallyl)cyclohex-2-en-1-yl)allyl acetate (16)



43 **16**

To a solution of diastereomeric alcohols **43** (3.06 g; 6.70 mmol) in dichloromethane (34 mL), were added acetic anhydride (1.30 mL; 1.40 g; 13.75 mmol; 2 eq.), triethylamine (2.80 mL; 2.03 g; 20.09 mmol; 3 eq.) and DMAP (166.7 mg; 1.36 mmol; 20 mol%), at room temperature. The reaction mixture was stirred for 24 h, then diluted with ethyl acetate (200 mL) and washed with water and brine. The organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5), to afford 3.25 g (97%) of diastereomeric allylic acetates **16**, as a colorless oil. A small sample of the diastereomeric allylic acetates **16** was separated for the spectral characterization.

Spectral data for the stereoisomer 1

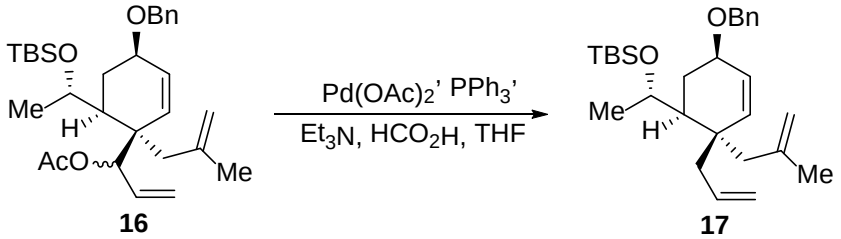
$\boldsymbol{R_f}$ = 0.32 (SiO_2, petroleum ether/ethyl acetate = 95:5).
$\boldsymbol{[\alpha]_D^{20}}$ –39.9 (*c* 1.04, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 4H), 7.33 – 7.28 (m, 1H), 6.01 – 5.91 (m, 2H), 5.59 (dd, *J* = 10.3, 2.1 Hz, 1H), 5.34 (d, *J* = 6.8 Hz, 1H), 5.27 – 5.23 (m, 1H), 5.23 – 5.18 (m, 1H), 4.86 (s, 1H), 4.68 – 4.59 (m, 3H), 4.23 (qd, *J* = 6.3, 3.4 Hz, 1H), 4.06 (ddt, *J* = 10.1, 6.1, 2.0 Hz, 1H), 2.37 (d, *J* = 13.9 Hz, 1H), 2.23 – 2.17 (m, 1H), 2.10 – 2.04 (m, 4H), 1.87 – 1.78 (m, 1H), 1.76 – 1.72 (m, 1H), 1.68 (s, 3H), 1.28 (d, *J* = 6.1 Hz, 3H), 0.95 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 169.4 (C), 143.0 (C), 139.1 (C), 134.6 (CH), 134.0 (CH), 131.2 (CH), 128.3 (2xCH), 127.51 (2xCH), 127.4 (CH), 117.9 (CH_2), 116.0 (CH_2), 78.5 (CH), 75.3 (CH_2), 69.5 (CH_2), 67.3 (CH), 45.0 (CH_2), 44.5 (C), 44.1 (CH),

26.8 (CH_2), 26.3 (3xCH_3), 24.5 (CH_3), 24.5 (CH_3), 21.5 (CH_3), 18.5 (C), -3.2 (CH_3), -3.5 (CH_3).
IR (ATR) *v* 3071, 3028, 2953, 2931, 2888, 2856, 1744, 1642, 1458, 1371, 1234, 1136, 1074, 1026, 939, 833, 778 cm^{-1}.
HRMS (ESI) calculated for $C_{30}H_{46}O_4SiNa^+$ $[M+Na]^+$: 521.3058, found: 521.3038.

Spectral data for the stereoisomer 2

R_f = 0.33 (SiO_2, petroleum ether/ethyl acetate = 95:5).
[α]$_D^{20}$ –91.6 (*c* 1.05, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.32 (m, 4H), 7.30 – 7.26 (m, 1H), 6.17 (ddd, *J* = 17.4, 10.9, 4.8 Hz, 1H), 5.90 – 5.84 (m, 1H), 5.60 (dd, *J* = 10.4, 2.2 Hz, 1H), 5.55 – 5.49 (m, 1H), 5.12 (dt, *J* = 10.9, 1.4 Hz, 1H), 5.04 (dt, *J* = 17.4, 1.6 Hz, 1H), 4.84 – 4.80 (m, 1H), 4.64 – 4.55 (m, 3H), 4.32 (qd, *J* = 6.2, 1.9 Hz, 1H), 4.00 (ddt, *J* = 9.9, 5.9, 2.0 Hz, 1H), 2.38 (d, *J* = 13.9 Hz, 1H), 2.27 (d, *J* = 13.8 Hz, 1H), 2.13 – 2.03 (m, 4H), 1.75 (dt, *J* = 13.7, 2.1 Hz, 1H), 1.72 – 1.62 (m, 4H), 1.22 (d, *J* = 6.2 Hz, 3H), 0.91 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9 (C), 143.6 (C), 139.0 (C), 136.8 (CH), 133.8 (CH), 130.7 (CH), 128.4 (2xCH), 127.6 (2xCH), 127.4 (CH), 115.8 (CH_2), 115.3 (CH_2), 78.0 (CH), 75.5 (CH), 69.7 (CH_2), 66.6 (CH), 45.8 (C), 45.2 (CH_2), 43.5 (CH_2), 26.2 (3xCH_3), 25.7 (CH_2), 24.1 (CH_3), 23.9 (CH_3), 21.0 (CH_3), 18.3 (C), -3.6 (CH_3), -3.8 (CH_3).
IR (ATR) *v* 3070, 3029, 2953, 2931, 2886, 2857, 1742, 1642, 1457, 1371, 1236, 1136, 1091, 1020, 944, 832, 777, 736 cm^{-1}.
HRMS (ESI) calculated for $C_{30}H_{46}O_4SiNa^+$ $[M+Na]^+$: 521.3058, found: 521.3039.

((*S*)-1-((1*S*,2*S*,5*R*)-2-Allyl-5-(benzyloxy)-2-(2-methylallyl)cyclohex-3-en-1-yl)ethoxy)(*tert*-butyl)dimethylsilane (17)



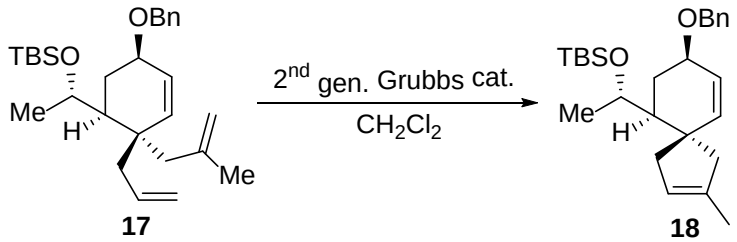
16 **17**

To a solution of palladium(II) acetate (186.1 mg; 0.83 mmol; 12.6 mol%) in dry THF (35 mL) was added triphenylphosphine (1.72 g; 6.56 mmol; 1 eq.) and the reaction mixture was stirred at room temperature for 30 min, under an argon atmosphere. The reaction mixture was cooled to 0 °C and triethylamine (36.5 mL; 26.5 g; 261.87 mmol; 40 eq.), 100% formic acid (9.9 mL; 12.08 g; 262.39 mmol; 40 eq.) and a solution of

allylic acetates **16** (3.27 g; 6.56 mmol) in THF (40 mL) were added dropwise in this order. The reaction mixture was stirred 4 h at 50 °C, before it was diluted with ethyl acetate (200 mL) and sucessively washed with 1.5 M HCl, sat. $NaHCO_{3\,(aq)}$ and brine. The organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 975:25), to afford 2.83 g (98%) of the titled compound **17**, as a colorless oil.

$\boldsymbol{R_f}$ = 0.52 (SiO_2, petroleum ether/ethyl acetate = 95:5).
$\boldsymbol{[\alpha]_D^{20}}$ –66.4 (*c* 1.01, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 4H), 7.30 – 7.25 (m, 1H), 5.89 – 5.78 (m, 1H), 5.75 – 5.70 (m, 1H), 5.60 (dd, *J* = 10.3, 2.0 Hz, 1H), 5.08 – 4.98 (m, 2H), 4.80 – 4.75 (m, 1H), 4.65 (d, *J* = 11.9 Hz, 1H), 4.60 (d, *J* = 11.9 Hz, 1H), 4.58 – 4.56 (m, 1H), 4.21 (q, *J* = 6.3 Hz, 1H), 4.04 (ddt, *J* = 10.1, 5.9, 1.9 Hz, 1H), 2.47 (dd, *J* = 13.4, 6.4 Hz, 1H), 2.26 – 2.18 (m, 2H), 2.11 (dd, *J* = 13.4, 8.7 Hz, 1H), 2.03 (ddt, *J* = 12.5, 5.6, 1.9 Hz, 1H), 1.73 – 1.58 (m, 5H), 1.14 (d, *J* = 6.2 Hz, 3H), 0.87 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 144.2 (C), 139.0 (C), 138.5 (CH), 135.0 (CH), 128.4 (2xCH), 128.0 (CH), 127.7 (2xCH), 127.4 (CH), 117.3 (CH_2), 114.7 (CH_2), 76.0 (CH), 70.0 (CH_2), 65.9 (CH), 46.2 (CH_2), 44.1 (CH), 43.8 (CH_2), 42.1 (C), 26.0 (3xCH_3), 24.7 (CH_2), 24.1 (CH_3), 23.6 (CH_3), 18.1 (C), -2.8 (CH_3), -4.6 (CH_3).
IR (ATR) *v* 3070, 3027, 2955, 2930, 2890, 2856, 1640, 1457, 1370, 1314, 1254, 1161, 1136, 1091, 1070, 1027, 1003, 948, 887, 833, 774, 736 cm^{-1}.
HRMS (ESI) calculated for $C_{28}H_{44}O_2SiNa^+$ $[M+Na]^+$: 463.3003, found: 463.3014.

((*S*)-1-((5*S*,6*S*,8*R*)-8-(Benzyloxy)-2-methylspiro[4.5]deca-2,9-dien-6-yl)ethoxy)(*tert*-butyl)dimethylsilane (18)



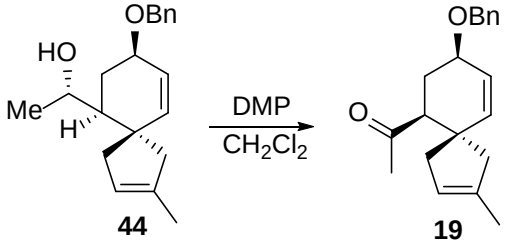
17 **18**

To a solution of compound **17** (2.83 g; 6.42 mmol) in dichloromethane (65 mL) was added 2nd generation Grubbs catalyst (109.0 mg; 0.13 mmol; 2 mol%) and the reaction

mixture was stirred for 30 min, at 45 ºC and under an argon atmosphere. The solvent was removed on rotovap and the residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5), to afford 2.56 g (97%) of the spirobicyclic compound **18**, as a colorless oil.

$\boldsymbol{R_f}$ = 0.48 (SiO_2, petroleum ether/ethyl acetate = 95:5).
$\boldsymbol{[\alpha]_D^{20}}$ +12.2 (*c* 0.98, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 4H), 7.29 – 7.25 (m, 1H), 5.68 (dd, *J* = 9.9, 2.0 Hz, 1H), 5.60 – 5.53 (m, 1H), 5.27 – 5.17 (m, 1H), 4.65 (d, *J* = 11.9 Hz, 1H), 4.59 (d, *J* = 11.9 Hz, 1H), 4.12 – 4.02 (m, 2H), 2.97 – 2.83 (m, 1H), 2.26 – 2.04 (m, 4H), 1.69 (s, 3H), 1.52 – 1.36 (m, 2H), 1.16 (d, *J* = 6.4 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 141.1 (CH), 139.0 (C), 137.5 (C), 128.3 (2xCH), 127.7 (2xCH), 127.4 (CH), 124.3 (CH), 124.2 (CH), 76.0 (CH), 69.8 (CH_2), 67.1 (CH), 50.8 (CH_2), 49.2 (CH), 46.0 (C), 40.5 (CH_2), 27.4 (CH_2), 26.0 (3xCH_3), 25.0 (CH_3), 18.1 (C), 16.4 (CH_3), -3.2 (CH_3), -4.9 (CH_3).
IR (ATR) *v* 3030, 2955, 2930, 2857, 1456, 1372, 1254, 1134, 1072, 1028, 946, 865, 834, 774, 736 cm^{-1}.
HRMS (ESI) calculated for $C_{26}H_{40}O_2SiNa^+$ $[M+Na]^+$: 435.2690, found: 435.2687.

1-((5*S*,6*S*,8*R*)-8-(Benzyloxy)-2-methylspiro[4.5]deca-2,9-dien-6-yl)ethan-1-one (19)

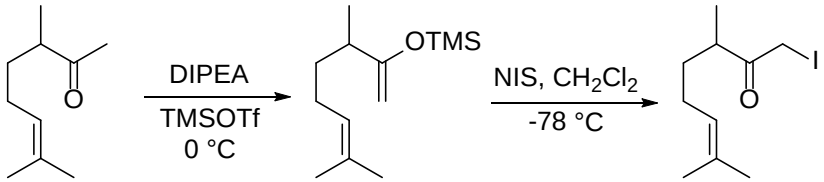


44 **19**

To a solution of alcohol **44** (73.0 mg; 0.24 mmol) in dichloromethane (4.9 mL) was added Dess-Martin periodinane (180.0 mg; 0.42 mmol; 1.75 eq.) and the reaction mixture was stirred for 1 hr at room temperature. The reaction mixture was diluted with dichloromethane and washed with 10% $Na_2S_2O_{3\,(aq)}$ and sat. $NaHCO_{3\,(aq)}$. The organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 8:2), to afford 69.0 mg (95%) of the methyl ketone **19**, as a colorless oil.

R_f = 0.52 (SiO_2, petroleum ether/ethyl acetate = 8:2).
$[\alpha]_D^{20}$ +36.7 (*c* 1.18, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 4H), 7.29 – 7.25 (m, 1H), 5.71 (dd, *J* = 10.0, 1.7 Hz, 1H), 5.65 (dt, *J* = 10.1, 1.6 Hz, 1H), 5.14 (bs, 1H), 4.60 (d, *J* = 11.8 Hz, 1H), 4.54 (d, *J* = 11.8 Hz, 1H), 4.06 (ddt, *J* = 9.4, 5.6, 1.9 Hz, 1H), 2.62 (dd, *J* = 12.4, 2.4 Hz, 1H), 2.60 – 2.52 (m, 1H), 2.48 – 2.42 (m, 1H), 2.41 – 2.35 (m, 1H), 2.28 – 2.21 (m, 1H), 2.13 (s, 3H), 2.08 – 2.01 (m, 1H), 1.86 (td, *J* = 12.7, 9.5 Hz, 1H), 1.66 (bs, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 210.2 (C), 139.2 (CH), 138.5 (C), 138.4 (C), 128.3 (2xCH), 127.6 (2xCH), 127.5 (CH), 125.6 (CH), 124.2 (CH), 73.6 (CH), 69.9 (CH_2), 55.1 (CH), 50.9 (CH_2), 47.2 (C), 41.3 (CH_2), 30.8 (CH_3), 29.5 (CH_2), 16.4 (CH_3).
IR (ATR) *v* 3382, 3086, 3028, 2930, 2848, 1702, 1496, 1448, 1354, 1322, 1275, 1207, 1184, 1092, 1071, 1023, 754 cm^{-1}.
HRMS (ESI) calculated for $C_{20}H_{24}O_2Na^+$ $[M+Na]^+$: 319.1668, found: 319.1662.

1-Iodo-3,7-dimethyloct-6-en-2-one (20)



20

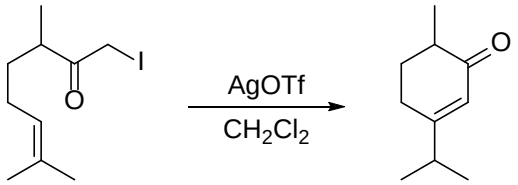
To a cold (0 °C) solution of 3,7-dimethyloct-6-en-2-one[5] (500 mg; 3.24 mmol) and diisopropylethylamine (1.46 g; 11.34 mmol; 3.5 eq.) in dry dichloromethane (6.5 mL) trimethylsilyl trifluoromethanesulfonate (1.80 g; 8.1 mmol; 2.5 eq.) was added, under an argon atmosphere. After stirring for 90 min at 0 °C, the resulting mixture was partitioned between hexane and sat. $NaHCO_{3\,(aq)}$. The organic phase was washed with water and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was used in the next step without further purification.

To a cold (-78 °C) solution of the crude silyl enol ether (733 mg; 3.24 mmol) in dry dichloromethane (32.0 mL) *N*-iodosuccinimide (801 mg; 3.56 mmol; 1.1 eq.) was added, under an argon atmosphere. After stirring for 45 min at -78 °C, 10% $Na_2S_2O_{3\,(aq)}$ was added and the reaction mixture was extracted with diethyl ether. The organic extract was washed with sat. $NaHCO_{3\,(aq)}$ and brine, dried over anh. $MgSO_4$, filtered and

concentrated under reduced pressure. The crude product was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 975 : 25), to provide 717 mg (79%) of 1-iodo-3,7-dimethyloct-6-en-2-one **20**, as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.07 – 5.04 (m, 1H), 3.86 (d, J = 10.0 Hz, 1H), 3.83 (d, J = 10.5 Hz, 1H), 2.92 (h, J = 6.5 Hz, 1H), 2.00 – 1.93 (m, 2H), 1.77 – 1.69 (m, 1H), 1.67 (s, 3H), 1.58 (s, 3H), 1.43 – 1.36 (m, 1H), 1.15 (d, J = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ: 206.5, 132.7, 123.6, 43.3, 33.6, 25.8, 25.8, 17.9, 17.4, 6.0.
IR (ATR) ν 2968, 2928, 1705, 1455, 1378, 1250, 1163, 1019 cm^{-1}.

3-Isopropyl-6-methylcyclohex-2-enone (21)

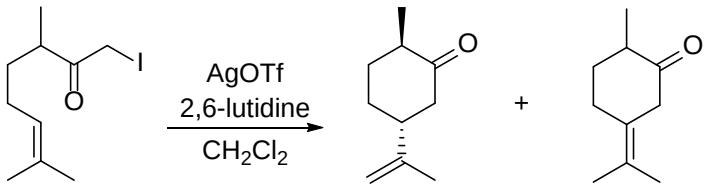


20 **21**

To a solution of 1-iodo-3,7-dimethyloct-6-en-2-one **20** (20.0 mg; 0.071 mmol) in dry dichloromethane (1.0 mL) silver trifluoromethanesulfonate (27.5 mg; 0.107 mmol; 1.5 eq.) was added, under an argon atmosphere. After stirring for 30 min at room temperature, the reaction mixture was filtered through a short pad of celite and the filtrate was carefully concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 9:1) afforded 8.1 mg (74%) of 3-isopropyl-6-methylcyclohex-2-enone **21**, as a colorless film.[6]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.84 (d, J = 1.0 Hz, 1H), 2.39 (dt, J = 7.0, 14.0 Hz, 1H), 2.34 – 2.28 (m, 3H), 2.06 (ddd, J = 4.5, 9.0, 17.5 Hz, 1H), 1.70 – 1.62 (m, 1H), 1.13 (d, J = 7.0 Hz, 3H), 1.10 (d, J = 2.0 Hz, 3H), 1.08 (d, J = 2.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ: 202.9, 170.9, 123.2, 41.2, 35.6, 31.2, 27.4, 21.0, 20.7, 15.3.

***trans*-2-Methyl-5-(prop-1-en-2-yl)cyclohexanone (22) and 2-methyl-5-(propan-2-ylidene)cyclohexanone (23)**

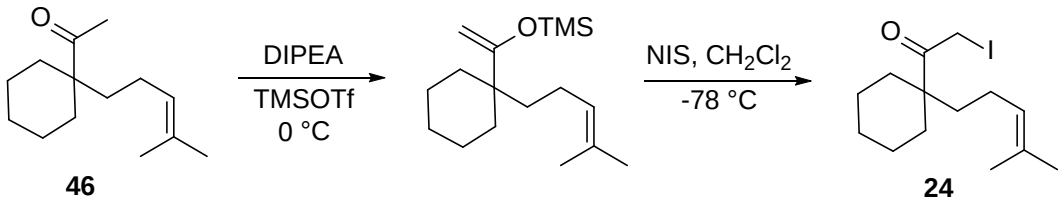


20 **22** **23**

To a solution of 1-iodo-3,7-dimethyloct-6-en-2-one **20** (50.0 mg; 0.178 mmol) and 2,6-lutidine (22.9 mg; 0.214 mmol; 1.2 eq.) in dry dichloromethane (3.0 mL), silver trifluoromethanesulfonate (68.8 mg; 0.268 mmol; 1.5 eq.) was added, under an argon atmosphere. After stirring for 15 min at room temperature, the reaction mixture was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 9:1) afforded 19.5 mg (72% combined yield) of an inseparable mixture of regioisomers **22** and **23** (1:1), as a colorless film.[7]

^{1}H NMR (500 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **22**): 4.74 (t, J = 1.5 Hz, 1H), 4.71 (s, 1H), 2.43 (dt, J = 2.5, 11.5 Hz, 1H), 2.39 – 2.23 (m, 3H), 2.04 – 1.98 (m, 1H), 1.95 – 1.89 (m, 1H), 1.72 (s, 3H), 1.64 – 1.61 (m, 1H), 1.37 – 1.29 (m, 1H), 1.01 (d, J = 6.5 Hz, 3H). δ (compound **23**): 3.30 (d, J = 15.5 Hz, 1H), 2.92 (d, J = 15.5 Hz, 1H), 2.70 (dt, J = 4.0, 15.0 Hz, 1H), 2.39 – 2.23 (m, 1H), 2.20 – 2.08 (m, 2H), 1.66 (s, 3H), 1.63 (s, 3H), 1.37 – 1.29 (m, 1H), 1.04 (d, J = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ: 212.7, 211.8, 147.8, 126.3, 125.1, 109.7, 47.1, 47.0, 46.2, 44.9, 44.7, 35.0, 32.9, 30.9, 28.5, 20.6, 20.4, 20.1, 14.9, 14.5.

2-Iodo-1-(1-(4-methylpent-3-enyl)cyclohexyl)ethanone (24)



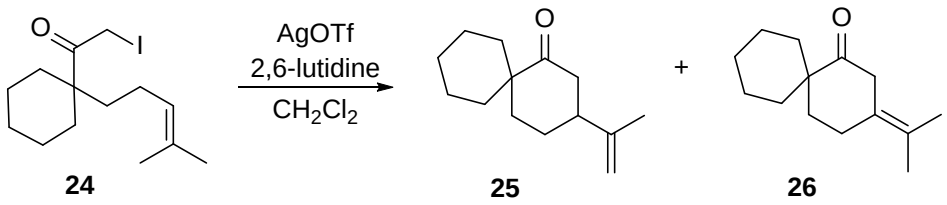
46 **24**

To a cold (0 °C) solution of 1-(1-(4-methylpent-3-enyl)cyclohexyl)ethanone **46** (175 mg; 0.84 mmol) and diisopropylethylamine (380 mg; 2.94 mmol; 3.5 eq.) in dry dichloromethane (2.5 mL), trimethylsilyl trifluoromethanesulfonate (467 mg; 2.1 mmol; 2.5 eq.) was added, under an argon atmosphere. After stirring for 90 min at 0 °C, the resulting mixture was partitioned between hexane and sat. $NaHCO_{3\ (aq)}$. The organic phase was washed with water and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was used in the next step without further purification.

To a cold (-78 °C) solution of the crude silyl enol ether (235 mg; 0.84 mmol) in dry dichloromethane (5.0 mL), *N*-iodosuccinimide (208 mg; 0.924 mmol; 1.1 eq.) was added, under an argon atmosphere. After stirring for 45 min at -78 °C, 10% $Na_2S_2O_{3\ (aq)}$ was added and the reaction mixture was extracted with diethyl ether. The organic extract was washed with sat. $NaHCO_{3\ (aq)}$ and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5), to provide 276 mg (98%) of 2-iodo-1-(1-(4-methylpent-3-enyl)cyclohexyl)ethanone **24**, as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.03 – 4.97 (m, 1H), 4.04 (s, 2H), 2.05 – 1.97 (m, 2H), 1.81 – 1.74 (m, 2H), 1.65 (d, J = 1.0 Hz, 3H), 1.57 – 1.53 (m, 7H), 1.51 – 1.46 (m, 1H), 1.39 – 1.27 (m, 5H).
^{13}C NMR (126 MHz, $CDCl_3$) δ: 206.8, 132.5, 123.6, 52.7, 39.3, 33.9 (2 x C), 26.0, 25.8, 23.1 (2 x C), 22.9, 17.8, 4.9.
IR (ATR) ν 2930, 2855, 1707, 1452, 1380, 1215, 1020 cm^{-1}.
HRMS (ESI) calculated for $C_{14}H_{24}IO^+$ $[M+H]^+$: 335.0866, found: 335.0869.

3-(Prop-1-en-2-yl)spiro[5.5]undecan-1-one (25) and 3-(propan-2-ylidene)spiro[5.5]undecan-1-one (26)

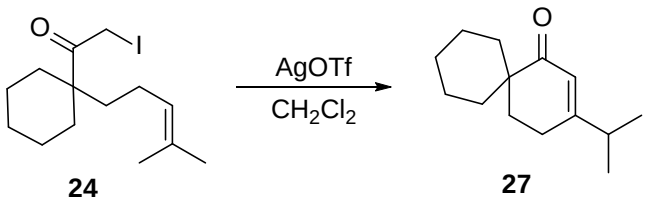


24 **25** **26**

To a solution of 2-iodo-1-(1-(4-methylpent-3-enyl)cyclohexyl)ethanone **24** (100.0 mg; 0.299 mmol) and 2,6-lutidine (44.8 mg; 0.418 mmol; 1.4 eq.) in dry dichloromethane (6.0 mL), silver trifluoromethanesulfonate (93.0 mg; 0.362 mmol; 1.2 eq.) was added, under an argon atmosphere. After stirring for 60 min at room temperature, the reaction mixture was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2; eluent petroleum ether/ethyl acetate = 98:2) afforded 55.3 mg (89% combined yield) of an inseparable mixture of regioisomers **25** and **26** (1:1.25), as a colorless film.

^{1}H NMR (500 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **25**): 4.71 (s, 1H), 4.69 (s, 1H), 2.53 (t, J = 12.5 Hz, 1H), 2.31 – 2.26 (m, 1H), 2.24 (ddd, J = 1.5, 4.0, 12.5 Hz, 1H), 1.95 (dt, J = 4.0, 13.5 Hz, 1H), 1.88 – 1.77 (m, 1H), 1.76 – 1.63 (m, 7H), 1.55 – 1.30 (m, 7H), 1.28 – 1.21 (m, 1H). δ (compound **26**): 3.11 (s, 2H), 2.34 (t, J = 6.5 Hz, 2H), 1.88 – 1.77 (m, 1H), 1.76 – 1.63 (m, 3H), 1.62 (s, 3H), 1.60 (s, 3H), 1.55 – 1.30 (m, 7H), 1.13 – 1.06 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$ data read from the spectrum of the regioisomeric mixture) δ: 216.1, 215.1, 147.7, 125.5, 124.8, 109.8, 48.3, 47.8, 47.0, 43.5, 43.3, 37.0, 33.8, 33.6, 33.1, 32.7 (2 x C), 26.3, 26.1, 25.7, 24.3, 22.2, 22.0, 21.8 (2 x C), 20.6, 20.3, 20.0.
IR (ATR) ν 2928, 2856, 1706, 1668, 1449, 1373, 1278, 1218, 1161 cm^{-1}.
HRMS (ESI) calculated for $C_{14}H_{23}O^+$ $[M+H]^+$: 207.1743, found: 207.1743.

3-Isopropylspiro[5.5]undec-2-en-1-one (27)

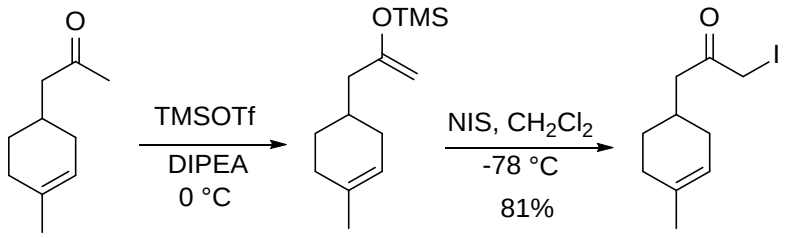


24 **27**

To a solution of 2-iodo-1-(1-(4-methylpent-3-enyl)cyclohexyl)ethanone **24** (49.0 mg; 0.146 mmol) in dry dichloromethane (3.0 mL), silver trifluoromethanesulfonate (45.2 mg; 0.176 mmol; 1.2 eq.) was added, under an argon atmosphere. After stirring for 60 min at room temperature, the reaction mixture was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 9:1) afforded 27.0 mg (90%) of 3-isopropylspiro[5.5]undec-2-en-1-one **27**, as a colorless film.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.74 (bs, 1H), 2.36 (dt, J = 7.0, 14.0 Hz, 1H), 2.27 (td, J = 1.0, 6.0 Hz, 2H), 1.88 (t, J = 6.5 Hz, 2H), 1.71 – 1.50 (m, 5H), 1.45 – 1.28 (m, 5H), 1.74 (d, J = 7.0 Hz, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ: 205.5, 168.6, 122.6, 43.7, 35.4, 31.6 (2 x C), 30.8, 26.2, 24.4, 21.7 (2 x C), 20.9 (2 x C).
IR (ATR) ν 2925, 2859, 1666, 1630, 1451, 1424, 1359, 1293, 1214 cm^{-1}.
HRMS (ESI) calculated for $C_{14}H_{23}O^+$ $[M+H]^+$: 207.1743, found: 207.1738.

1-Iodo-3-(4-methylcyclohex-3-enyl)propan-2-one (28)



47 **28**

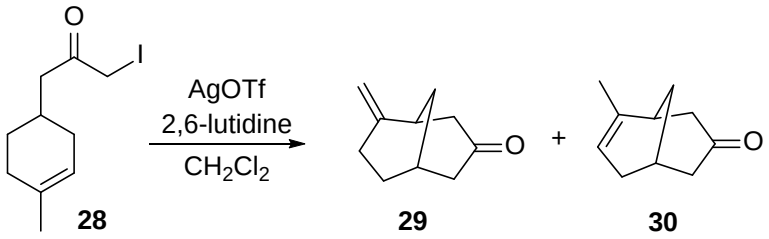
To a cold (0 °C) solution of 1-(4-methylcyclohex-3-enyl)propan-2-one **47** (240 mg; 1.56 mmol) and diisopropylethylamine (705 mg; 5.45 mmol; 3.5 eq.) in dry dichloromethane (6.0 mL), trimethylsilyl trifluoromethanesulfonate (870 mg; 3.90

mmol; 2.5 eq.) was added, under an argon atmosphere. After stirring for 90 min at 0 °C, the resulting mixture was partitioned between hexane and sat. $NaHCO_{3\,(aq)}$. The organic phase was washed with water and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was used in the next step without further purification.

To a cold (-78 °C) solution of the crude silyl enol ether (350 mg; 1.56 mmol) in dry dichloromethane (7.8 mL) *N*-iodosuccinimide (386 mg; 1.71 mmol; 1.1 eq.) was added, under an argon atmosphere. After stirring for 45 min at -78 °C, 10% $Na_2S_2O_{3\,(aq)}$ was added and the reaction mixture was extracted with diethyl ether. The organic extract was washed with sat. $NaHCO_{3\,(aq)}$ and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5), to provide 350 mg (81%) of 1-iodo-3-(4-methylcyclohex-3-enyl)propan-2-one **28**, as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.31 (bs, 1H), 3.78 (s, 2H), 2.53 (d, J = 6.5 Hz, 2H), 2.12 – 1.97 (m, 3H), 1.94 – 1.87 (m, 1H), 1.75 – 1.62 (m, 2H), 1.63 (s, 3H), 1.33 – 1.25 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ: 202.7, 133.9, 119.8, 45.8, 31.5, 29.7, 29.6, 28.8, 23.6, 7.0.
IR (ATR) ν 2928, 1710, 1439, 1364, 1270, 1162, 1038 cm^{-1}.
HRMS (ESI) calculated for $C_{10}H_{16}IO^+$ $[M+H]^+$: 279.0240, found: 279.0237.

6-Methylenebicyclo[3.3.1]nonan-3-one (29) and 6-methylbicyclo[3.3.1]non-6-en-3-one (30)



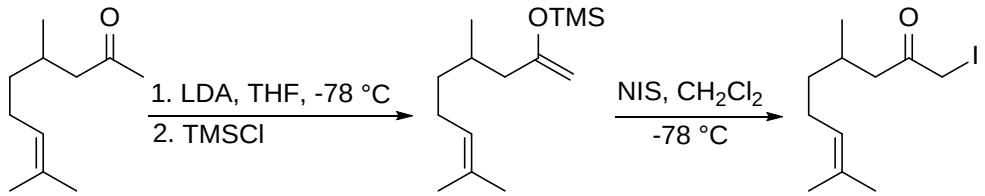
28 **29** **30**

To a solution of 1-iodo-3-(4-methylcyclohex-3-enyl)propan-2-one **28** (50.3 mg; 0.180 mmol) and 2,6-lutidine (32.9 mg; 0.307 mmol; 1.7 eq.) in dry dichloromethane (3.6 mL), silver trifluoromethanesulfonate (69.7 mg; 0.271 mmol; 1.5 eq.) was added, under

an argon atmosphere. After stirring for 6 h at room temperature, the reaction mixture was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 85:15) afforded 23.7 mg (88% combined yield) of an inseparable mixture of regioisomers **29** and **30** (1:1.7), as a colorless film.

^{1}H NMR (500 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **29**): 4.67 (t, J = 2.0 Hz, 1H), 4.60 (t, J = 2.0 Hz, 1H), 2.89 (bs, 1H), 2.55 – 2.30 (m, 4H), 2.25 – 1.72 (m, 6H), 1.69 – 1.63 (m, 1H). δ (compound **30**): 5.28 (bs, 1H), 2.55 – 2.30 (m, 7H), 2.25 – 1.72 (m, 3H), 1.61 (t, J = 1.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ: 212.4, 211.6, 150.9, 136.5, 119.9, 107.8, 49.2, 48.0, 47.2, 44.8, 40.7, 35.8, 34.5, 33.3, 32.8, 30.9, 30.3, 29.6, 28.1, 22.1.
IR (ATR) ν 2925, 2858, 1710, 1648, 1446, 1414, 1227, 1170, 937 cm^{-1}.
HRMS (ESI) calculated for $C_{10}H_{15}O^+$ $[M+H]^+$: 151.1117, found: 151.1118.

1-Iodo-4,8-dimethylnon-7-en-2-one (31)



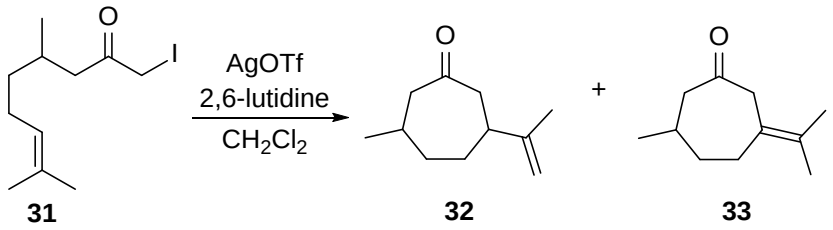
31

To a cold (0 °C) solution of diisopropylamine (198 mg; 1.96 mmol; 1.1 eq.) in dry THF (5.0 mL), *n*-butyl lithium was added (1.37 mL; 1.4 M in hexanes; 1.96 mmol; 1.1 eq.), under an argon atmosphere. The solution was stirred for 10 min at that temperature, cooled to -78 °C, and then the solution of 4,8-dimethylnon-7-en-2-one (300 mg; 1.78 mmol) in THF (2 mL) was added dropwise, over 5 min. After the addition was complete, the reaction mixture was stirred for 1 h at -78 °C, when TMSCl (232 mg; 2.13 mmol; 1.2 eq.) was added dropwise. The reaction mixture was stirred at -78 °C for 1 h and then partitioned between hexane and sat. $NaHCO_{3\ (aq)}$. The organic phase was washed with water and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was used in the next step without further purification.

To a cold (-78 °C) solution of the crude silyl enol ether (427 mg; 1.78 mmol) in dry dichloromethane (19.0 mL) *N*-iodosuccinimide (441 mg; 1.96 mmol; 1.1 eq.) was added, under an argon atmosphere. After stirring for 45 min at -78 °C, 10% $Na_2S_2O_{3\,(aq)}$ was added and the reaction mixture was extracted with diethyl ether. The organic extract was washed with sat. $NaHCO_{3\,(aq)}$ and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5), to provide 412 mg (81%) of 1-iodo-4,8-dimethylnon-7-en-2-one **31**, as a dark yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.08 – 5.03 (m, 1H), 3.77 (d, J = 5.5 Hz, 1H), 3.75 (d, J = 5.5 Hz, 1H), 2.69 (dd, J = 5.5, 16.5 Hz, 1H), 2.50 (dd, J = 8.0, 16.5 Hz, 1H), 2.05 – 1.89 (m, 3H), 1.65 (s, 3H), 1.57 (s, 3H), 1.34 – 1.28 (m, 1H), 1.23 – 1.16 (m, 1H), 0.89 (d, J = 6.5 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ:202.8, 131.7, 124.2, 46.7, 36.8, 29.1, 25.8, 25.5, 19.6, 17.8, 7.0.
IR (ATR) ν 2962, 2922, 1708, 1454, 1407, 1378, 1183, 1026 cm^{-1}.
HRMS (ESI) calculated for $C_{11}H_{20}IO^+$ $[M+H]^+$: 295.0553, found: 295.0549.

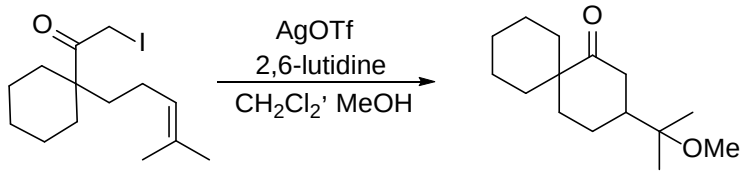
3-Methyl-6-(prop-1-en-2-yl)cycloheptanone (32) and 3-methyl-6-(propan-2-ylidene)cycloheptanone (33)



To a solution of 1-iodo-4,8-dimethylnon-7-en-2-one **31** (100.0 mg; 0.34 mmol) and 2,6-lutidine (43.7 mg; 0.408 mmol; 1.2 eq.) in dry dichloromethane (6.0 mL), silver trifluoromethanesulfonate (131.1 mg; 0.510 mmol; 1.5 eq.) was added, under an argon atmosphere. After stirring for 30 min at room temperature, the reaction mixture was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5) afforded 39.6 mg (67% combined yield) of an inseparable mixture of regioisomers **32** and **33** (1.9/1), as a colorless film.[8]

^{1}H NMR (500 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **32**): 4.70 (m, 1H), 4.68 (t, J = 1.5 Hz, 1H), 2.60 – 2.56 (m, 1H), 2.50 – 2.35 (m, 3H), 2.35 – 2.25 (m, 1H), 1.94 – 1.80 (m, 3H), 1.70 (s, 3H), 1.50 – 1.44 (m, 1H), 1.30 – 1.20 (m, 1H), 1.00 (d, J = 6.5 Hz, 3H). δ (compound **33**): 3.31 (d, J = 16.5 Hz, 1H), 3.16 (d, J = 16.5 Hz, 1H), 2.60 – 2.56 (m, 1H), 2.35 – 2.25 (m, 2H), 1.94 – 1.80 (m, 4H), 1.73 (s, 3H), 1.68 (s, 3H), 0.98 (d, J = 6.5 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ: 213.3, 212.3, 149.7, 128.8, 125.5, 109.6, 52.2, 51.2, 49.4 (2 x C), 44.1, 38.5, 38.0, 35.4, 32.5, 32.4, 31.8, 24.3, 23.6, 20.7, 20.2, 20.1.
IR (ATR) ν 2955, 2925, 1698, 1455, 1378, 1281, 1163 cm^{-1}.
HRMS (ESI) calculated for $C_{11}H_{19}O^+$ $[M+H]^+$: 167.1430, found: 167.1431.

3-(2-Methoxypropan-2-yl)spiro[5.5]undecan-1-one (34)

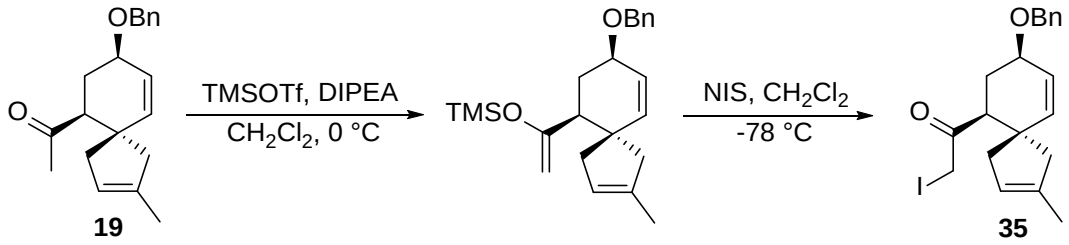


24 **34**

To a solution of 2-iodo-1-(1-(4-methylpent-3-enyl)cyclohexyl)ethanone **24** (50.0 mg; 0.149 mmol) and 2,6-lutidine (35.3 mg; 0.329 mmol; 2.2 eq.) in a mixture of dichloromethane/methanol (5.0 mL, 9/1), silver trifluoromethanesulfonate (65.0 mg; 0.254 mmol; 1.7 eq.) was added, under an argon atmosphere. After stirring for 12 h at room temperature, the reaction mixture was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. Purification of the crude residue by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 9:1) afforded 14.6 mg (41%) of 3-(2-methoxypropan-2-yl)spiro[5.5]undecan-1-one **34**, as a colorless film.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.15 (s, 3H), 2.45 (t, J = 13.5 Hz, 1H), 2.23 – 2.19 (m, 1H), 2.00 (dt, J = 3.5, 14.0 Hz, 1H), 1.90 – 1.74 (m, 3H), 1.72 – 1.62 (m, 3H), 1.58 – 1.48 (m, 2H), 1.45 – 1.21 (m, 5H), 1.13 – 1.04 (m, 4H), 1.15 (d, J = 1.5 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ: 217.1, 75.8, 49.1, 48.4, 48.2, 39.7, 37.1, 33.8, 33.5, 26.4, 22.5, 22.4, 22.2, 22.1, 21.3.
IR (ATR) ν 2932, 2854, 1703, 1450, 1364, 1230, 1136, 1076 cm^{-1}.
HRMS (ESI) calculated for $C_{15}H_{26}NaO_2^+$ $[M+Na]^+$: 261.1830, found: 261.1823.

1-((5*S*,6*S*,8*R*)-8-(Benzyloxy)-2-methylspiro[4.5]deca-2,9-dien-6-yl)-2-iodoethan-1-one (35)



19 **35**

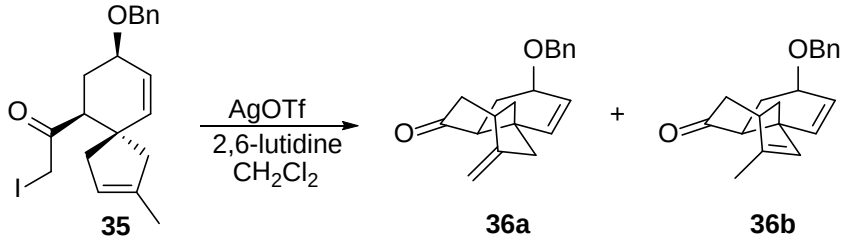
To a cold (0 °C) solution of methyl ketone **19** (153.1 mg; 0.52 mmol) in dichloromethane (10 mL), trimethylsilyl triflate (0.51 mL; 0.63 mg; 2.82 mmol; 5.4 eq.) and diisopropylethylamine (0.63 mL; 0.47 mg; 3.62 mmol; 7 eq.) were added and the reaction mixture was stirred for 3 h, under an argon atmosphere. The reaction was quenched with sat. $NaHCO_{3\,(aq)}$ and the mixture was extracted three times with diethyl ether. The organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The crude silyl enol ether was used in the next step without further purification.

N-iodosuccinimide (141.0 mg; 0.63 mmol; 1.2 eq.) was added to a cold (-78 °C) solution of the crude silyl enol ether (~190.4 mg; 0.52 mmol) in dichloromethane (5 mL) and the reaction mixture was stirred at that temperature for 30 min, under an argon atmosphere. The reaction was quenched with a mixture of sat. $NaHCO_{3\,(aq)}$ and 10% $Na_2S_2O_{3\,(aq)}$ (v/v = 1:1) and the product was extracted with dichloromethane. The organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5), to afford 215.0 mg (93%, after 2 steps) of the titled compound **35**, as a pale yellow oil.

$\boldsymbol{R_f}$ = 0.32 (SiO_2, petroleum ether/ethyl acetate = 95:5).
$\boldsymbol{[\alpha]_D^{20}}$ +123.8 (*c* 1.03, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 4H), 7.31 – 7.25 (m, 1H), 5.74 – 5.68 (m, 2H), 5.16 (bs, 1H) 4.60 (d, *J* = 11.6 Hz, 1H), 4.54 (d, *J* = 11.7 Hz, 1H), 4.13 – 4.06 (m, 1H), 3.83 (d, *J* = 10.0 Hz, 1H), 3.76 (d, *J* = 10.0 Hz, 1H), 3.05 (dd, *J* = 11.9, 2.6 Hz, 1H), 2.59 – 2.51 (m, 1H), 2.51 – 2.44 (m, 1H), 2.35 – 2.27 (m, 2H), 2.10 – 2.03 (m, 1H), 1.96 (ddd, *J* = 13.1, 11.8, 9.2 Hz, 1H), 1.67 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 203.6 (C), 138.5 (CH), 138.4 (C), 138.2 (C), 128.4 (2xCH), 127.7 (2xCH), 127.6 (CH), 126.2 (CH), 125.5 (CH), 73.2 (CH), 70.0 (CH_2), 51.5 (CH_2), 51.2 (CH), 48.0 (C), 41.3 (CH_2), 30.6 (CH_2), 16.5 (CH_3), 8.4 (CH_2).
IR (ATR) *v* 3394, 3026, 2940, 2845, 2735, 1706, 1658, 1496, 1447, 1382, 1345, 1315, 1267, 1213, 1177, 1090, 941, 899, 804, 752 cm^{-1}.
HRMS (ESI) calculated for $C_{20}H_{23}O_2INa^+$ $[M+Na]^+$: 445.0635, found: 445.0636.

(2*R*,4a*S*,7*S*,9a*S*)-2-(Benzyloxy)-6-methylene-1,5,6,7,8,9a-hexahydro-4a,7-methanobenzo[7]annulen-9(2*H*)-one (36a) and (2*R*,4a*R*,7*S*,9a*S*)-2-(benzyloxy)-6-methyl-1,7,8,9a-tetrahydro-4a,7-methanobenzo[7]annulen-9(2*H*)-one (36b)



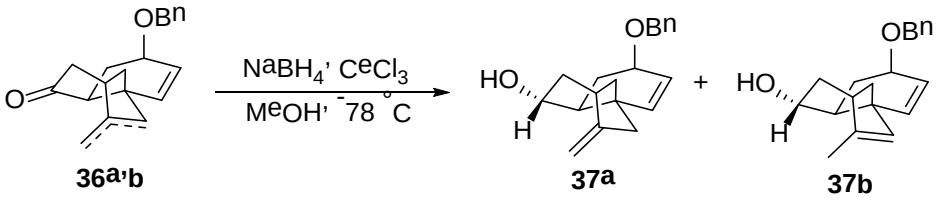
35 **36a** **36b**

To a solution of iodoketone **35** (177.8 mg; 0.42 mmol) in dichloromethane (7.0 mL) were added 2,6-lutidine (50.6 mg; 55 µL; 0.47 mmol) and silver triflate (168.1 mg: 0.65 mmol) and the reaction mixture was stirred at rt for 5 min, under an argon atmosphere. The reaction was quenched with sat. $NaHCO_{3\,(aq)}$ and the product was extracted with dichloromethane (3x). The combined organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by column chromatography (SiO_2; eluent: benzene/ethyl acetate = 95:5), to afford 115.1 mg (93%) of a mixture of alkenes **36a,b** (**36a/36b =** 1/3), as a colorless oil.

R_f = 0.46 (SiO_2, benzene/ethyl acetate = 95:5).
^{1}H NMR (500 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **36a**): 7.38 – 7.31 (m, 4H), 7.31 – 7.26 (m, 1H), 5.82 – 5.77 (m, 1H), 5.56 (dd, *J* = 10.2, 2.1 Hz, 1H), 5.00 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.95 (d, *J* = 2.3 Hz, 1H), 4.66 – 4.60 (m, 1H), 4.57 – 4.52 (m, 1H), 4.19 – 4.12 (m, 1H), 2.98 – 2.90 (m, 1H), 2.51 – 2.44 (m, 2H), 2.40 – 2.38 (m, 1H), 2.34 – 2.28 (m, 2H), 2.28 – 2.20 (m, 1H), 1.91 (dd, *J* = 12.3, 2.7 Hz, 1H), 1.88 – 1.82 (m, 1H), 1.78 – 1.69 (m, 1H). δ (compound **36b**): 7.38 – 7.31 (m, 4H), 7.31 – 7.26 (m, 1H), 5.82 – 5.77 (m, 1H), 5.66 (dd, *J* = 10.1, 2.1 Hz, 1H), 5.31 (s, 1H), 4.66 – 4.60 (m, 1H), 4.57 – 4.52 (m, 1H), 4.19 – 4.12 (m, 1H), 2.61 – 2.55 (m, 1H), 2.51 – 2.44 (m, 1H), 2.44 – 2.40 (m, 2H), 2.28 – 2.20 (m, 1H), 2.04 – 1.97 (m, 1H), 1.88 – 1.82 (m, 1H), 1.74 (d, *J* = 1.6 Hz, 3H), 1.65 – 1.56 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **36a**): 213.6 (C), 152.3 (C), 138.3 (C), 135.2 (CH), 129.6 (CH), 128.4 (2xCH), 127.7 (2xCH), 127.6 (CH), 108.8 (CH_2), 74.4 (CH), 70.5 (CH_2), 55.2 (CH), 49.8 (CH_2), 46.9 (CH_2), 44.5 (C), 40.6 (CH), 40.5 (CH_2), 31.3 (CH_2). δ (compound **36b**): 213.7 (C), 147.1 (C), 138.4 (C), 133.6 (CH), 132.9 (CH), 129.8 (CH), 128.4 (2xCH), 127.7 (2xCH), 127.6 (CH), 74.3 (CH), 70.3 (CH_2), 51.6 (CH), 48.0 (C), 44.0 (CH_2), 43.3 (CH_2), 41.8 (CH), 31.3 (CH_2), 15.1 (CH_3).
IR (ATR) *v* 3384, 3062, 3028, 2933, 2866, 1703, 1656, 1496, 1452, 1403, 1307, 1250, 1200, 1160, 1143, 1092, 1070, 1024, 967, 824, 738, 700 cm^{-1}.
HRMS (ESI) calculated for $C_{20}H_{22}O_2Na^+$ $[M+Na]^+$: 317.1512, found: 317.1509.

(2*R*,4a*S*,9*S*,9a*S*)-2-(Benzyloxy)-6-methylene-1,2,5,6,7,8,9,9a-octahydro-4a,7-methanobenzo[7]annulen-9-ol (37a) and (2*R*,4a*R*,9*S*,9a*S*)-2-(benzyloxy)-6-methyl-1,2,7,8,9,9a-hexahydro-4a,7-methanobenzo[7]annulen-9-ol (37b)



36a,b **37a** **37b**

To a cold (-78 °C) solution of a mixture of ketones **36a,b** (32.0 mg; 0.108 mmol) in methanol (1.0 mL), were added cerium(III) chloride heptahydrate (48.0 mg; 0.13 mmol; 1.2 eq.) and sodium borohydride (5.0 mg; 0.13 mmol; 1.2 eq.). The reaction mixture was stirred for 1 h at this temperature, diluted with diethyl ether and washed with sat. $NH_4Cl_{(aq)}$ and brine. The organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 7:3), to afford 27.1 mg (85%) of alcohols **37a,b** (**37a/37b =** 1/3), as a colorless oil. The isomers were separated for spectral characterization.

Spectral data for the regioisomer **37a**

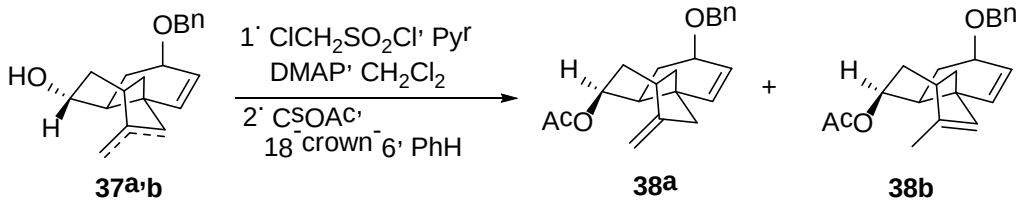
***R*$_f$** = 0.45 (SiO_2, petroleum ether/ethyl acetate = 7:3).
[α]$_D^{20}$ +7.1 (*c* 0.30, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 4H), 7.30 – 7.26 (m, 1H), 5.71 (dt, *J* = 10.0, 1.8 Hz, 1H), 5.57 (dd, *J* = 9.9, 1.9 Hz, 1H), 4.92 – 4.87 (m, 1H), 4.81 (bs, 1H), 4.65 (d, *J* = 11.8 Hz, 1H), 4.57 (d, *J* = 11.8 Hz, 1H), 4.19 – 4.07 (m, 2H), 2.70 – 2.66

(m, 1H), 2.38 (ddt, *J* = 12.1, 6.2, 1.8 Hz, 1H), 2.28 – 2.21 (m, 2H), 2.03 – 1.94 (m, 1H), 1.91 – 1.84 (m, 1H), 1.64 (dd, *J* = 11.9, 1.8 Hz, 1H), 1.54 – 1.39 (m, 3H), 1.28 (d, *J* = 5.6 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) *δ* 154.0 (C), 138.7 (C), 137.4 (CH), 128.8 (CH), 128.4 (2xCH), 127.7 (2xCH), 127.5 (CH), 105.1 (CH_2), 75.8 (CH), 70.1 (CH_2), 66.7 (CH), 45.6 (C), 45.0 (CH_2), 44.6 (CH), 41.8 (CH), 40.8 (CH_2), 39.9 (CH_2), 24.9 (CH_2).
IR (ATR) *ν* 3428, 3065, 3020, 2963, 2930, 2856, 1657, 1451, 1401, 1334, 1062, 1026, 976, 871, 743 cm^{-1}.
HRMS (ESI) calculated for $C_{20}H_{23}O_2^-$ $[M–H]^-$: 295.1704, found: 295.1696.

Spectral data for the regioisomer **37b**

R_f = 0.38 (SiO_2, petrol ether/ethyl acetate = 7:3).
[α]$_D^{20}$ +5.8 (*c* 0.20, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.39 – 7.31 (m, 4H), 7.29 – 7.26 (m, 1H), 5.72 (dt, *J* = 9.9, 1.5 Hz, 1H), 5.68 (dd, *J* = 10.0, 1.7 Hz, 1H), 5.19 (bs, 1H), 4.65 (d, *J* = 11.8 Hz, 1H), 4.57 (d, *J* = 11.8 Hz, 1H), 4.14 (ddt, *J* = 9.7, 6.3, 1.7 Hz, 1H), 3.97 – 3.88 (m, 1H), 2.48 – 2.41 (m, 1H), 2.39 – 2.34 (m, 1H), 2.00 – 1.88 (m, 2H), 1.77 – 1.71 (m, 4H), 1.66 (d, *J* = 10.8 Hz, 1H), 1.49 (ddd, *J* = 14.0, 12.1, 9.7 Hz, 1H), 1.29 – 1.19 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) *δ* 144.1 (C), 138.8 (C), 136.0 (CH), 129.4 (CH), 128.6 (CH), 128.4 (CH), 127.7 (2xCH), 127.5 (2xCH), 75.9 (CH), 70.0 (CH_2), 68.0 (CH), 50.2 (C), 46.0 (CH_2), 42.9 (CH), 38.4 (CH), 32.1 (CH_2), 26.1 (CH_2), 15.4 (CH_3).
IR (ATR) *ν* 3445, 3041, 3016, 2936, 2856, 1462, 1448, 1402, 1335, 1313, 1062, 1032, 972, 811, 748 cm^{-1}.
HRMS (ESI) calculated for $C_{20}H_{23}O_2^-$ $[M–H]^-$: 295.1704, found: 295.1695.

(2*R*,9*S*)-2-(Benzyloxy)-6-methylene-1,2,5,6,7,8,9,9a-octahydro-4a,7-methanobenzo[7]annulen-9-yl acetate (38a) and (2*R*,9*S*)-2-(Benzyloxy)-6-methyl-1,2,7,8,9,9a-hexahydro-4a,7-methanobenzo[7]annulen-9-yl acetate (38b)



37a,b **38a** **38b**

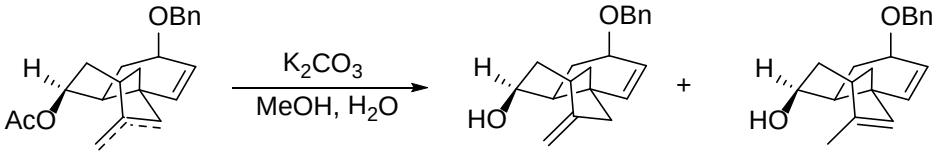
To a solution of alcohols **37a,b** (6.0 mg; 0.020 mmol) in dry dichloromethane (0.2 mL) 2,6-lutidine (6.5 mg; 0.060 mmol; 3.0 eq.), chloromethanesulfonyl chloride (4.5 mg;

0.030 mmol; 1.5 eq.) and DMAP (cat. amount) were added at 0 °C, under an argon atmosphere. After stirring for 30 min at room temperature, the reaction mixture was diluted with diethyl ether and the organic phase was washed with sat. $NaHCO_{3\,(aq)}$ and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude mixture of chloromesylates was used in the next step without further purification.

To a solution of the crude chloromesylates (8.2 mg; 0.020 mmol) in dry benzene (0.4 mL), cesium acetate (19.0 mg; 0.100 mmol; 5.0 eq.) and 18-crown-6 (5.3 mg; 0.020 mmol; 1.0 eq.) were added at room temperature, under an argon atmosphere. After stirring overnight at room temperature, the reaction mixture was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. Purification of the crude residue by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 85:15) afforded 2.8 mg (41%) of the acetates **38a,b** (**38a**/**38b**=1/10), as a colorless film.

^{1}H NMR (500 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **38b**): 7.37 – 7.31 (m, 5H), 7.29 – 7.26 (m, 1H), 5.73 (bd, J = 10.5 Hz, 1H), 5.60 (dd, J = 2.0, 10.5 Hz, 1H), 5.20 (s, 1H), 4.78 (d, J = 6.5 Hz, 1H), 4.61 (d, J = 11.5 Hz, 1H), 4.56 (d, J = 11.5 Hz, 1H), 4.15 – 4.09 (m, 1H), 2.31 – 2.27 (m, 1H), 2.26 – 2.22 (m, 1H), 2.02 – 1.96 (m, 1H), 1.97 (s, 3H), 1.82 – 1.77 (m, 1H), 1.75 (d, J = 1.0 Hz, 1H), 1.67 – 1.60 (m, 4H), 1.59 – 1.54 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **38b**): 170.6 (C), 146.8 (C), 138.8 (C), 135.8 (CH), 132.5 (CH), 128.6 (CH), 128.5 (CH), 127.8 (CH), 127.7 (CH), 75.2 (CH), 75.1 (CH), 70.3 (CH_2), 48.1 (C), 44.0 (CH_2), 42.3 (CH), 39.7 (CH), 33.4 (CH_2), 31.0 (CH_2), 21.5 (CH_3), 15.7 (CH_3).
IR (ATR) ν 3442, 3028, 2937, 1730, 1453, 1369, 1247, 1070, 1023 cm^{-1}.
HRMS (ESI) calculated for $C_{22}H_{26}NaO_3^+$ $[M+Na]^+$: 361.1780, found: 361.1783.

(2*R*,9*S*)-2-(Benzyloxy)-6-methylene-1,2,5,6,7,8,9,9a-octahydro-4a,7-methanobenzo[7]annulen-9-ol (39a) and (2*R*,9*S*)-2-(Benzyloxy)-6-methyl-1,2,7,8,9,9a-hexahydro-4a,7-methanobenzo[7]annulen-9-ol (39b)

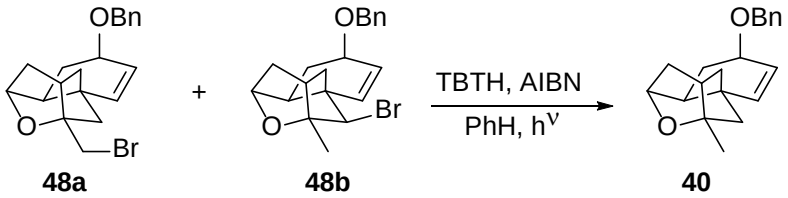


38a,b **39a** **39b**

To a solution of acetates **38a,b** (6.0 mg; 0.017 mmol) in a mixture of methanol and water (0.9 mL; 2:1) potassium carbonate (7.4 mg; 0.053 mmol; 3.0 eq.) was added. After stirring overnight at room temperature, the reaction mixture was diluted with diethyl ether and the organic phase was washed with sat. $NaHCO_{3\,(aq)}$ and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 7:3) afforded 4.0 mg (76%) of the alcohols **39a,b** (**39a**/**39b**=1/10), as a colorless film.

^{1}H NMR (500 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **39b**): 7.37 – 7.32 (m, 4H), 7.29 – 7.27 (m, 1H), 5.74 (d, J = 10.0 Hz, 1H), 5.62 (dd, J = 2.0, 10.0 Hz, 1H), 5.38 (s, 1H), 4.62 (d, J = 11.5 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.17 – 4.13 (m, 1H), 3.66 (t, J = 8.0 Hz, 1H), 2.35 – 2.31 (m, 1H), 2.23 – 2.18 (m, 1H), 2.02 – 1.94 (m, 2H), 1.86 – 1.73 (m, 3H), 1.83 (d, J = 1.5 Hz, 3H), 1.68 (d, J = 11.0 Hz, 1H), 1.66 – 1.61 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$, data read from the spectrum of the regioisomeric mixture) δ (compound **39b**): 149.4 (C), 138.8 (C), 135.7 (CH), 133.4 (CH), 128.8 (CH), 128.5 (CH), 127.8 (CH), 127.7(CH), 75.2 (CH), 73.7 (CH), 70.3 (CH_2), 48.4 (C), 44.8 (CH_2), 43.3 (CH), 42.8 (CH), 34.8 (CH_2), 33.9 (CH_2), 16.0 (CH_3).
IR (ATR) ν 3446, 3062, 2961, 1448, 1400, 1337, 1028 cm^{-1}.
HRMS (ESI) calculated for $C_{20}H_{223}O_2^-$ [M-H]$^-$: 295.1704, found: 295.1696.

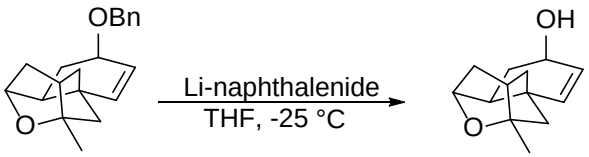
(3*R*,4a*S*,5*S*,8*S*,9a*S*)-3-(Benzyloxy)-8-methyl-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulene (40)



To a degased solution of bromides **48a,b** (24.0 mg; 0.06 mmol) in benzene (1.2 mL) tributyltin hydride (93.0 mg; 86.0 µL; 0.32 mmol; 5.3 eq.) and AIBN (1.0 mg; 0.01 mmol) were added, under an argon atmosphere. The reaction mixture was irradiated with a visible light (250 W Xenophot lamp) for 15 min. The reaction mixture was concentrated on rotovap and the residue was purified by column chromatography (SiO_2; eluent: benzene/ethyl acetate = 9:1), to afford 18.8 mg (99%) of debrominated compound **40**, as a colorless oil.

***R*$_f$** = 0.50 (SiO_2, petroleum ether/ethyl acetate = 7:3).
[α]$_D^{20}$ +32.2 (*c* 1.02, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 4H), 7.30 – 7.26 (m, 1H), 5.69 (dt, *J* = 10.0, 1.7 Hz, 1H), 5.45 (dd, *J* = 10.1, 1.9 Hz, 1H), 4.61 (d, *J* = 11.8 Hz, 1H), 4.56 (d, *J* = 11.8 Hz, 1H), 4.19 (ddt, *J* = 10.0, 6.1, 2.0 Hz, 1H), 4.12 (t, *J* = 3.7 Hz, 1H), 2.18 (t, *J* = 6.4 Hz, 1H), 1.98 – 1.92 (m, 2H), 1.89 – 1.83 (m, 1H), 1.80 (d, *J* = 11.2 Hz, 1H), 1.74 (dd, *J* = 11.1, 3.4 Hz, 1H), 1.67 (dd, *J* = 11.9, 3.5 Hz, 1H), 1.63 – 1.58 (m, 1H), 1.57 – 1.51 (m, 1H), 1.49 (d, *J* = 11.1 Hz, 1H), 1.38 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 138.6 (C), 135.4 (CH), 128.4 (CH), 128.4 (2xCH), 127.7 (2xCH), 127.5 (CH), 86.9 (C), 80.2 (CH), 75.7 (CH), 70.2 (CH_2), 52.1 (CH_2), 46.0 (C), 44.6 (CH_2), 44.6 (CH), 42.0 (CH), 38.3 (CH_2), 29.2 (CH_2), 23.3 (CH_3).
IR (ATR) *v* 3083, 3062, 3022, 2942, 2864, 1644, 1496, 1450, 1378, 1325, 1306, 1154, 1088, 1070, 1031, 1001, 975, 933, 823, 737 cm^{-1}.
HRMS (ESI) calculated for $C_{20}H_{25}O_2^+$ $[M+H]^+$: 297.1849, found: 297.1850.

(3*R*,4a*S*,5*S*,8*S*,9a*S*)-8-Methyl-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-3-ol (41)

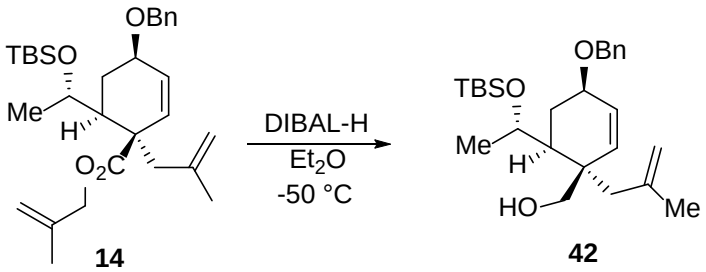


40 **41**

To a cold (-25 °C) solution of benzyl ether **40** (4.5 mg; 0.015 mmol) in dry THF (0.9 mL), a solution of lithium naphthalenide[9] was added dropwise, under an argon atmosphere, until a green color persisted for 2-3 min. The reaction was quenched with sat. $NH_4Cl_{(aq)}$ and the reaction mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 1:1), to provide 2.8 mg (90%) of the allylic alcohol **41**, as a colorless film.

$\boldsymbol{R_f}$ = 0.27 (SiO_2, petroleum ether/ethyl acetate = 1:1).
[α]$_D^{20}$ +9.5 (*c* 0.25, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.58 (dt, *J* = 10.0, 1.7 Hz, 1H), 5.42 (dd, *J* = 10.0, 2.0 Hz, 1H), 4.40 (ddt, *J* = 10.1, 6.3, 2.0 Hz, 1H), 4.13 (t, *J* = 4.0 Hz, 1H), 2.19 (t, *J* = 6.3 Hz, 1H), 2.01 – 1.95 (m, 1H), 1.93 – 1.83 (m, 2H), 1.80 (d, *J* = 11.2 Hz, 1H), 1.76 (dd, *J* = 11.2, 3.2 Hz, 1H), 1.67 – 1.63 (m, 1H), 1.62 – 1.59 (m, 1H), 1.50 (d, *J* = 11.1 Hz, 1H), 1.47 – 1.40 (m, 1H), 1.39 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 135.2 (CH), 130.8 (CH), 87.0 (C), 80.0 (CH), 69.1 (CH), 52.1 (CH_2), 45.8 (C), 44.7 (CH and CH_2), 42.1 (CH), 38.3 (CH_2), 32.7 (CH_2), 23.3 (CH_3).
IR (ATR) *v* 3396, 3013, 2944, 2866, 1448, 1379, 1326, 1286, 1154, 1089, 1057, 1020, 821, 747 cm^{-1}.
HRMS (ESI) calculated for $C_{13}H_{19}O_2^+$ $[M+H]^+$: 207.1380, found: 297.1378.

((1*R*,4*R*,6*S*)-4-(Benzyloxy)-6-((*S*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl)-1-(2-methylallyl)cyclohex-2-en-1-yl)methanol (42)

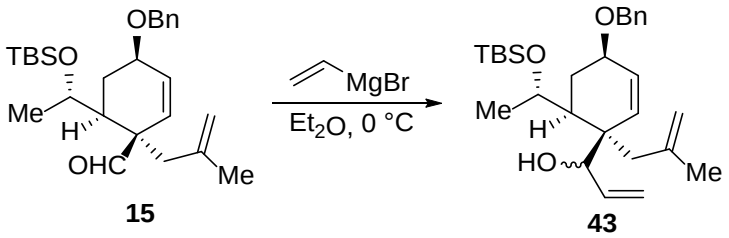


14 **42**

DIBAL-H (31 mL; 1.0 M in toluene; 31.00 mmol; 3 eq) was added dropwise over 15 minutes to a cold (-50 °C) solution of ester **14** (5.18 g; 10.38 mmol) in diethyl ether (65 mL), under an argon atmosphere. The reaction mixture was stirred at this temperature for 1 h, before the reaction was quenched by a slow addition of saturated solution of Rochelle salt (100 mL). The biphasic mixture was stirred vigorously for 2 h at room temperature, the organic layer was separated and the aqueous layer was extracted with diethyl ether (3 x 250 mL). The combined organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 9:1), to afford 3.87 g (87%) of the alcohol **42**, as white crystals.

m.p. 83-84 °C
R_f = 0.33 (SiO_2, petroleum ether/ethyl acetate = 9:1).
$[\alpha]_D^{20}$ –23.8 (*c* 1.04, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 4H), 7.31 – 7.24 (m, 1H), 5.85 (dt, *J* = 10.4, 1.7 Hz, 1H), 5.48 (dd, *J* = 10.2, 2.0 Hz, 1H), 4.85 – 4.79 (m, 1H), 4.64 – 4.60 (m, 3H), 4.48 (q, *J* = 6.5 Hz, 1H), 4.06 (ddt, *J* = 10.0, 5.9, 2.0 Hz, 1H), 3.60 (dd, *J* = 16.8, 10.3 Hz, 1H), 3.40 – 3.30 (m, 2H), 2.53 (d, *J* = 13.7 Hz, 1H), 2.06 (d, *J* = 13.7 Hz, 1H), 2.04 – 1.97 (m, 1H), 1.75 – 1.67 (m, 4H), 1.59 (dd, *J* = 13.3, 2.3 Hz, 1H), 1.25 (d, *J* = 6.5 Hz, 3H), 0.91 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4 (C), 138.9 (C), 136.5 (CH), 130.1 (CH), 128.4 (2xCH), 127.6 (2xCH), 127.5 (CH), 115.0 (CH_2), 75.7 (CH), 70.0 (CH_2), 67.6 (CH), 66.8 (CH_2), 44.3 (C), 44.2 (CH), 43.5 (CH_2), 26.1 (3xCH_3), 25.3 (CH_2), 24.6 (CH_3), 22.9 (CH_3), 18.4 (C), -2.3 (CH_3), -3.5 (CH_3).
IR (ATR) *v* 3460, 3068, 3028, 2954, 2932, 2886, 2857, 1641, 1458, 1372, 1317, 1256, 1135, 1065, 1030, 944, 889, 834, 775, 754 cm^{-1}.
HRMS (ESI) calculated for $C_{26}H_{42}O_3SiNa^+$ $[M+Na]^+$: 453.2795, found: 453.2779.

1-((1*R*,4*R*,6*S*)-4-(Benzyloxy)-6-((*S*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl)-1-(2-methylallyl)cyclohex-2-en-1-yl)prop-2-en-1-ol (43)



15 **43**

To a cold (0 °C) solution of aldehyde **15** (3.61 g, 8.42 mmol) in diethyl ether (84 mL), vinylmagnesium bromide (24 mL; 1M in THF; 24.00 mmol; 2.85 eq.) was added dropwise over 15 minutes, under an argon atmosphere. The reaction mixture was stirred for 30 min at 0 °C, before it was quenched by a slow addition of sat. $NH_4Cl_{(aq)}$. The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 x 100 mL). The combined organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 975:25), to afford 3.08 g (80%) of the diastereomeric alcohols **43**, as a colorless oil (*dr* = 10:1). The isomers were separated for spectral characterization.

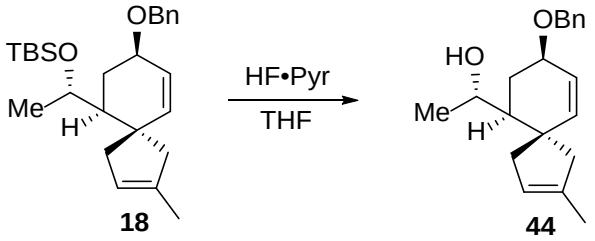
Spectral data for the major stereoisomer

***R*$_f$** = 0.25 (SiO_2, petroleum ether/ethyl acetate = 95:5).
[α]$_D^{20}$ –34.8 (*c* 1.00, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.30 (m, 4H), 7.27 – 7.23 (m, 1H), 6.03 – 5.98 (m, 1H), 5.94 (ddd, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.54 (dd, *J* = 10.4, 2.2 Hz, 1H), 5.25 (ddd, *J* = 17.2, 2.1, 1.3 Hz, 1H), 5.19 (ddd, *J* = 10.4, 2.0, 1.0 Hz, 1H), 4.81 – 4.77 (m, 1H), 4.64 (d, *J* = 12.1 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.58 – 4.52 (m, 1H), 4.41 (q, *J* = 6.3 Hz, 1H), 4.16 – 4.11 (m, 1H), 4.06 – 4.01 (m, 1H), 3.74 (d, *J* = 4.5 Hz, 1H), 2.18 (d, *J* = 13.8 Hz, 1H), 2.10 – 1.97 (m, 3H), 1.74 (dd, *J* = 11.8, 4.9 Hz, 1H), 1.63 (s, 3H), 1.25 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9 (C), 139.1 (C), 136.6 (CH), 133.8 (CH), 131.6 (CH), 128.3 (2xCH), 127.5 (2xCH), 127.3 (CH), 116.9 (CH_2), 115.1 (CH_2), 78.6 (CH), 75.4 (CH), 69.5 (CH_2), 67.3 (CH), 45.9 (C), 45.3 (CH_2), 43.5 (CH), 26.1 (CH_2), 26.0 (3xCH_3), 24.2 (CH_3), 23.1 (CH_3), 18.4 (C), -3.2 (CH_3), -4.0 (CH_3).
IR (ATR) *v* 3479, 3070, 3027, 2932, 2886, 2858, 1643, 1458, 1373, 1318, 1257, 1165, 1129, 1092, 1071, 1006, 938, 890, 834, 782, 736 cm^{-1}.
HRMS (ESI) calculated for $C_{28}H_{44}O_3SiNa^+$ $[M+Na]^+$: 479.2952, found: 479.2934.

Spectral data for the minor stereoisomer

***R*$_f$** = 0.37 (SiO_2, petroleum ether/ethyl acetate = 95:5).
[α]$_D^{20}$ –49.4 (*c* 1.00, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.40 – 7.33 (m, 4H), 7.31 – 7.26 (m, 1H), 5.89 (ddd, *J* = 16.8, 10.7, 5.7 Hz, 1H), 5.77 – 5.71 (m, 1H), 5.50 (dd, *J* = 10.3, 1.9 Hz, 1H), 5.31 (dt, *J* = 17.1, 1.8 Hz, 1H), 5.18 (dt, *J* = 10.6, 1.7 Hz, 1H), 4.83 (d, *J* = 3.1 Hz, 1H), 4.81 – 4.77 (m, 1H), 4.66 – 4.58 (m, 4H), 4.44 – 4.37 (m, 1H), 4.11 – 4.05 (m, 1H), 2.90 (d, *J* = 14.1 Hz, 1H), 2.04 – 1.97 (m, 2H), 1.74 (td, *J* = 13.0, 10.1 Hz, 1H), 1.63 (s, 3H), 1.61 (dd, *J* = 13.1, 2.0 Hz, 1H), 1.25 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.16 (s, 3H), 0.16 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) *δ* 144.1 (C), 138.8 (CH), 138.8 (C), 136.7 (CH), 128.4 (CH), 128.4 (2xCH), 127.7 (2xCH), 127.6 (CH), 116.4 (CH_2), 115.0 (CH_2), 75.9 (CH), 74.2 (CH), 70.1 (CH_2), 68.4 (CH), 46.8 (C), 45.1 (CH), 38.9 (CH_2), 26.1 (3xCH_3), 24.7 (CH_2), 24.4 (CH_3), 22.7 (CH_3), 18.5 (C), -1.9 (CH_3), -3.2 (CH_3).
IR (ATR) *ν* 3400, 3071, 3028, 2950, 2932, 2882, 2857, 1643, 1463, 1378, 1304, 1256, 1134, 1090, 1072, 1023, 937, 898, 833, 776, 739 cm^{-1}.
HRMS (ESI) calculated for $C_{28}H_{44}O_3SiNa^+$ $[M+Na]^+$: 479.2952, found: 479.2934.

(*S*)-1-((5*S*,6*S*,8*R*)-8-(Benzyloxy)-2-methylspiro[4.5]deca-2,9-dien-6-yl)ethan-1-ol (44)



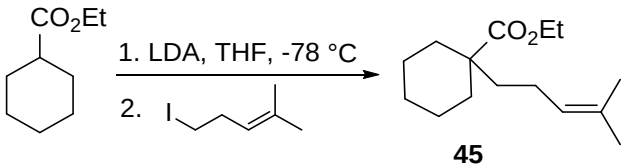
18 **44**

To a solution of silyl ether **18** (53.2 mg; 0.13 mmol) in tetrahydrofuran (0.65 mL), was added hydrogen fluoride pyridine complex (~70% hydrogen fluoride; 0.10 mL; 110.0 mg; 3.85 mmol; 30 eq.) and the reaction mixture was stirred at room temperature for 24 h. Saturated $NaHCO_{3\,(aq)}$ was added and the products was extracted with ethyl acetate, the organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 85:15), to afford 36.0 mg (94%) of alcohol **44**, as a colorless oil.

***R*$_f$** = 0.40 (SiO_2, petroleum ether/ethyl acetate = 8:2).
[α]$_D^{20}$ +51.0 (*c* 1.22, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 4H), 7.30 – 7.26 (m, 1H), 5.81 (dd, J = 10.1, 1.6 Hz, 1H), 5.62 (dd, J = 10.0, 2.6 Hz, 1H), 5.29 – 5.25 (m, 1H), 4.65 (d, J = 11.9 Hz, 1H), 4.60 (d, J = 11.9 Hz, 1H), 4.06 – 3.98 (m, 2H), 2.85 – 2.78 (m, 1H), 2.24 – 2.17 (m, 3H), 2.12 (d, J = 7.0 Hz, 1H), 2.10 – 2.03 (m, 1H), 1.80 (ddd, J = 13.3, 9.7, 7.4 Hz, 1H), 1.70 (s, 3H), 1.48 (dt, J = 9.7, 2.7 Hz, 1H), 1.22 (d, J = 6.5 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 141.5 (CH), 139.0 (C), 138.5 (C), 128.4 (2xCH), 127.6 (2xCH), 127.5 (CH), 123.7 (CH), 123.2 (CH), 73.6 (CH), 70.0 (CH_2), 66.6 (CH), 51.5 (CH_2), 47.5 (CH), 46.7 (C), 40.9 (CH_2), 25.5 (CH_2), 23.5 (CH_3), 16.5 (CH_3).
IR (ATR) ν 3436, 3086, 3062, 3029, 2962, 2911, 2860, 2732, 1714, 1650, 1496, 1451, 1375, 1322, 1259, 1091, 1070, 1024, 946, 908, 738, 698 cm^{-1}.
HRMS (ESI) calculated for $C_{20}H_{26}O_2Na^+$ $[M+Na]^+$: 321.1825, found: 321.1822.

Ethyl 1-(4-methylpent-3-enyl)cyclohexanecarboxylate (45)



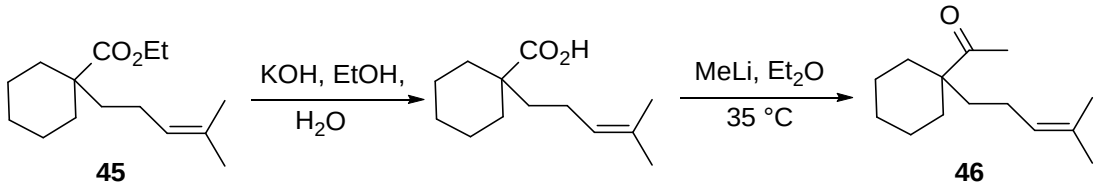
45

To a cold (0 °C) solution of diisopropylamine (1.80 g; 17.8 mmol; 1.1 eq.) in dry THF (15.0 mL) *n*-butyl lithium was added (14.85 mL; 1.2 M in hexanes; 17.8 mmol; 1.1 eq.), under an argon atmosphere. The solution was stirred for 10 min at that temperature, cooled to -78 °C, and then ethyl cyclohexanecarboxylate (2.50 g; 16.0 mmol) was added dropwise, over 15 min. After the addition was complete, the reaction mixture was stirred for 1 h at -78 °C, when a solution of 5-iodo-2-methylpent-2-ene[10] (3.70 g; 17.8 mmol; 1.1 eq.) in DMSO (3.0 mL) was added dropwise. The reaction mixture was stirred at -78 °C for 30 min, warmed up to room temperature and stirred overnight. The reaction was quenched with 1.5 M HCl and the organic phase was washed with water and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 975 : 25) to provide 3.0 g (78%) of ethyl 1-(4-methylpent-3-enyl)cyclohexanecarboxylate (**45**), as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.05 – 5.02 (m, 1H), 4.13 (q, J = 7.0 Hz, 2H), 2.06 (bd, J = 13.0 Hz, 2H), 1.88 – 1.83 (m, 2H), 1.65 (s, 3H), 1.58 – 1.51 (m, 3H), 1.56 (s, 3H), 1.49 – 1.46 (m, 2H), 1.38 – 1.28 (m, 2H), 1.25 (t, J = 7.0 Hz, 3H), 1.23 – 1.16 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ: 176.9, 131.7, 124.3, 60.1-, 46.8, 40.6, 34.2 (2 x C), 26.1, 25.8, 23.4 (2 x C), 22.9, 17.6, 14.5.
IR (ATR) ν 2930, 2857, 1696, 1453, 1244, 1199 cm^{-1}.
HRMS (ESI) calculated for $C_{15}H_{27}O_2^+$ $[M+H]^+$: 239.2006, found: 239.2006.

1-(1-(4-Methylpent-3-enyl)cyclohexyl)ethanone (46)



45 **46**

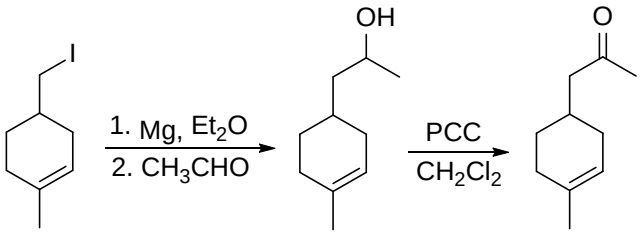
A solution of ethyl 1-(4-methylpent-3-enyl)cyclohexanecarboxylate (**45**) (2.50 g; 10.5 mmol) in ethanol (12 mL) was added to a solution of potassium hydroxide (1.76 g; 31.5 mmol; 3 eq.) in water (35 mL). Ethanol was added to the reaction mixture until the solution cleared up. The reaction mixture was stirred at 78 °C for 48 h. Ethanol was removed under reduced pressure and the aqueous solution of the potassium salt was washed diethyl ether, acidified with hydrochloric acid and extracted with diethyl ether. The organic layer was washed with water and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure, to give the crude acid (1.60 g, 73%), which was used in the next step without further purification.

To a cold (0 °C) solution of the crude acid (280 mg; 1.33 mmol) in dry diethyl ether (6.0 mL) methyl lithium (1.77 mL; 3.0 M in dimethoxymethane; 5.32 mmol; 4 eq.) was added dropwise, under an argon atmosphere. After the addition was complete, the reaction mixture was stirred for 2 h at 35 °C, and then slowly poured into cold 1 M $HCl_{(aq)}$. The organic phase was washed with water and brine, dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 95:5) to provide 200 mg (80%) of 1-(1-(4-methylpent-3-enyl)cyclohexyl)ethanone (**46**), as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.99 (t, J = 7.0 Hz, 1H), 2.07 (s, 3H), 1.99 – 1.92 (m, 2H), 1.77 – 1.69 (m, 2H), 1.63 (s, 3H), 1.56 – 1.49 (m, 2H), 1.52 (s, 3H), 1.49 – 1.43 (m, 3H), 1.29 – 1.22 (m, 5H).

^{13}C NMR (126 MHz, $CDCl_3$) δ: 213.5, 131.9, 124.0, 52.1, 39.1, 33.4 (2 x C), 26.2, 25.7, 25.2, 23.0 (2 x C), 22.6, 17.6.
IR (ATR) ν 2930, 2855, 1703, 1452, 1352, 1155, 1125 cm^{-1}.
HRMS (ESI) calculated for $C_{14}H_{25}O^+$ $[M+H]^+$: 209.1900, found: 209.1900.

1-(4-Methylcyclohex-3-enyl)propan-2-one (47)



47

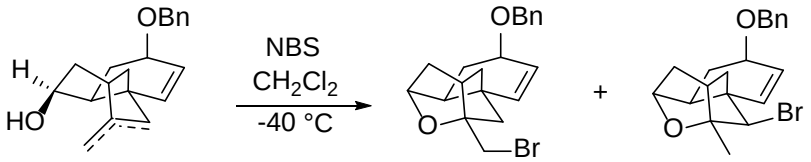
To a suspension of magnesium turnings (205 mg; 8.43 mmol; 1.1 eq.) in dry diethyl ether (10.0 mL), 4-(iodomethyl)-1-methylcyclohex-1-ene[11] (1.81 g; 7.67 mmol) was added dropwise over 20 min, at room temperature and under an argon atmosphere. The reaction mixture was refluxed for 1 h, followed by cooling to 0 °C. After cooling, a solution of acetaldehyde (506 mg; 11.5 mmol; 1.5 eq.) in diethyl ether (3.0 mL) was added in a dropwise manner, ensuring a low temperature is maintained. After stirring for 10 min at 0 °C, the reaction was quenched with sat. $NH_4Cl_{(aq)}$ and the mixture was extracted twice with diethyl ether. The combined organic layer was washed with brine, dried over anh. Na_2SO_4, and concentrated under reduced pressure, to give the crude alcohol, which was used in the next step without further purification.

To a solution of the crude alcohol (1.01 g) in dry dichloromethane (15.0 mL), PCC (205 mg; 8.43 mmol; 1.1 eq.) was added and the mixture was stirred for 2 h at rt. Diethyl ether was added to the reaction mixture, the resulting suspension was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. Purification of the crude product by dry flash chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 9:1), afforded 641 mg (55%) 1-(4-methylcyclohex-3-enyl)propan-2-one **47**, as a light yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.29 (bs, 1H), 2.34 (d, J = 6.5 Hz, 2H), 2.10 (s, 3H), 2.07 – 1.95 (m, 3H), 1.91 – 1.82 (m, 1H), 1.71 – 1.66 (m, 1H), 1.65 – 1.57 (m, 1H), 1.60 (s, 3H), 1.28 – 1.19 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ: 208.8, 133.9, 120.0, 50.3, 31.7, 30.4, 29.6, 29.5, 29.0, 23.6.
IR (ATR) ν 2928, 1710, 1439, 1364, 1270, 1162, 1038 cm^{-1}.
HRMS (ESI) calculated for $C_{10}H_{17}O^+$ $[M+H]^+$: 153.1274, found: 153.1273.

(3*R*,4a*S*,5*S*,8*R*,9a*S*)-3-(Benzyloxy)-9-bromo-8-methyl-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulene (48a) and

(3*R*,4a*S*,5*S*,8*S*,9a*S*)-3-(benzyloxy)-8-(bromomethyl)-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulene (48b)



39a,b **48a** **48b**

To a cold (-45 °C) solution of alcohols **39a,b** (55.7 mg; 0.19 mmol) in dichloromethane (3.8 mL), were added 4Å molecular sieves (100 mg) and NBS (34.0 mg; 0.19 mmol), under an argon atmosphere, and the reaction mixture was stirred for 30 min at this temperature. The reaction was quenched with a mixture of sat. $NaHCO_{3\ (aq)}$ and 10% $Na_2S_2O_{3\ (aq)}$ (v/v = 1/1) and the product was extracted with dichloromethane (3x). The organic extract was dried over anh. $MgSO_4$, filtered and concentrated on rotovap. The residue was purified by column chromatography (SiO_2; eluent: petroleum ether/ethyl acetate = 7:3), to afford 66.0 mg (93%) of mixture of bromides **48a,b** (**48a/48b =** 1/10), as a colorless oil. The major isomer was separated for the spectral characterization.

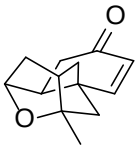
Spectral data for the major isomer (**48b**)

***R*$_f$** = 0.53 (SiO_2, petroleum ether/ethyl acetate = 7:3).
^{1}H NMR (500 MHz, $CDCl_3$, δ 7.39 – 7.32 (m, 4H), 7.31 – 7.27 (m, 1H), 5.82 (dd, J = 10.4, 1.8 Hz, 1H), 5.80 – 5.75 (m, 1H), 4.60 (d, J = 11.7 Hz, 1H), 4.57 (d, J = 11.8 Hz, 1H), 4.26 (d, J = 2.2 Hz, 1H), 4.19 – 4.12 (m, 2H), 2.47 – 2.40 (m, 1H), 2.25 (ddd, J = 6.9, 4.4, 2.1 Hz, 1H), 2.18 – 2.12 (m, 1H), 1.99 (ddt, J = 11.9, 6.0, 2.0 Hz, 1H), 1.93 –

1.88 (m, 2H), 1.69 (dd, *J* = 12.7, 2.2 Hz, 1H), 1.62 (ddd, *J* = 13.7, 12.3, 10.0 Hz, 1H), 1.55 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.4 (C), 132.5 (CH), 129.9 (CH), 128.4 (2xCH), 127.7 (3xCH), 90.8 (C), 80.3 (CH), 75.1 (CH), 71.5 (CH), 70.4 (CH_2), 50.8 (C), 45.1 (CH), 43.8 (CH), 41.5 (CH_2), 38.4 (CH_2), 29.2 (CH_2), 22.4 (CH_3).

Copies of ^{1}H and ^{13}C NMR spectra



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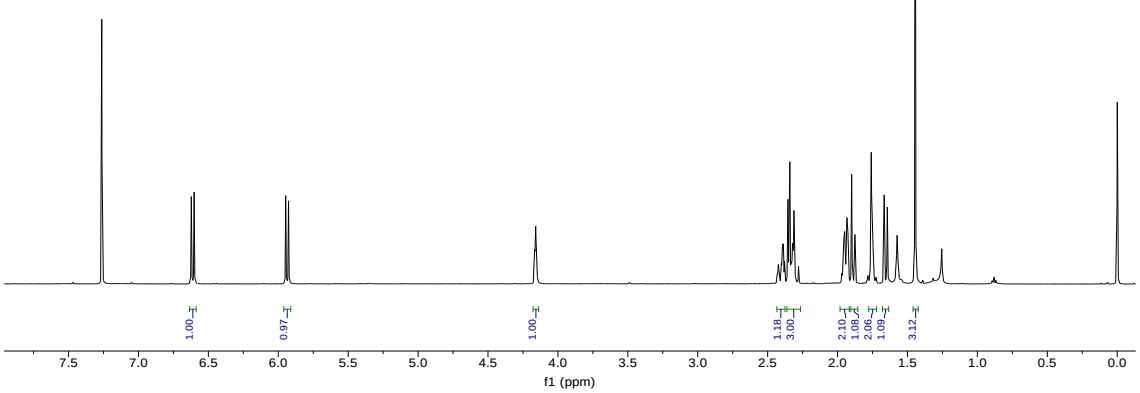

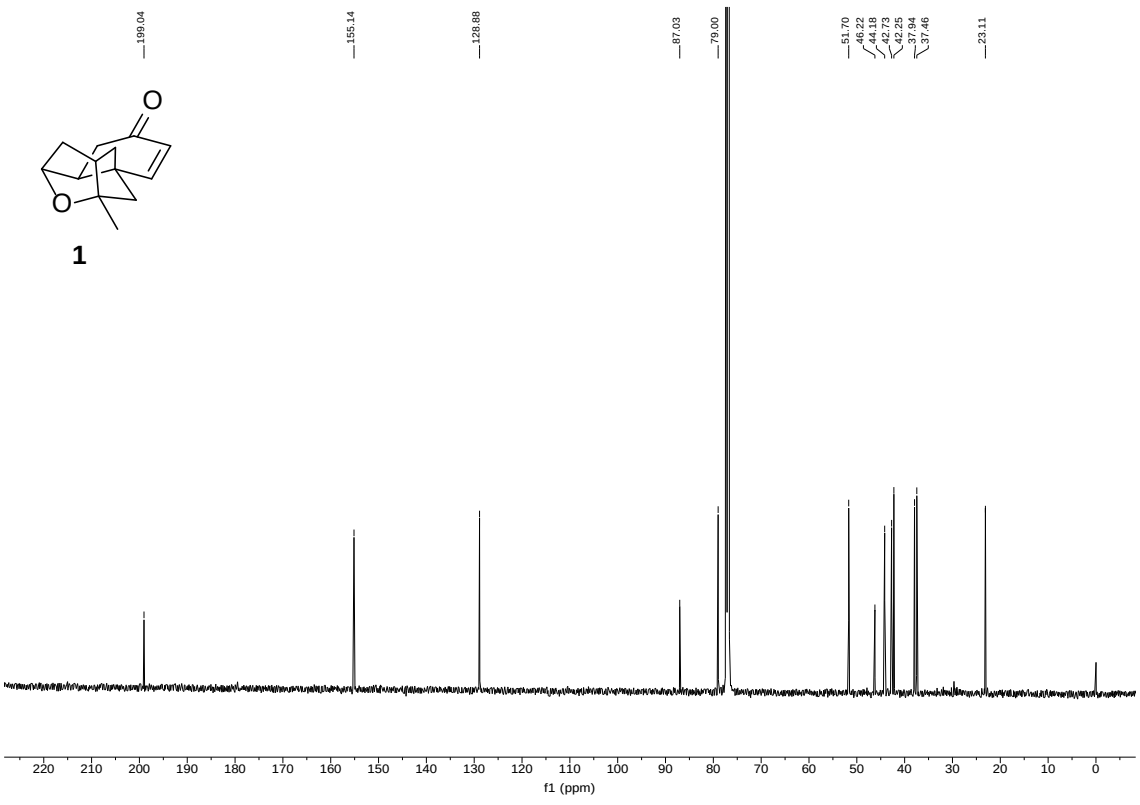

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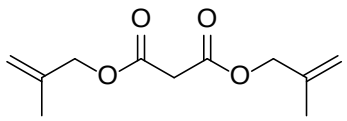
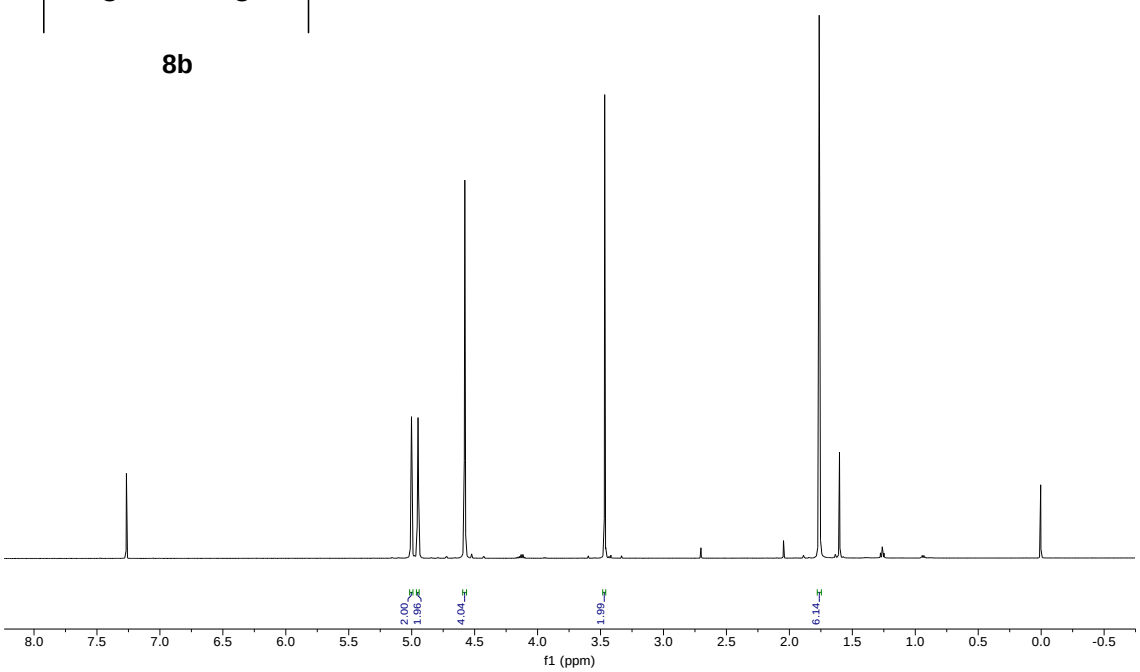


8b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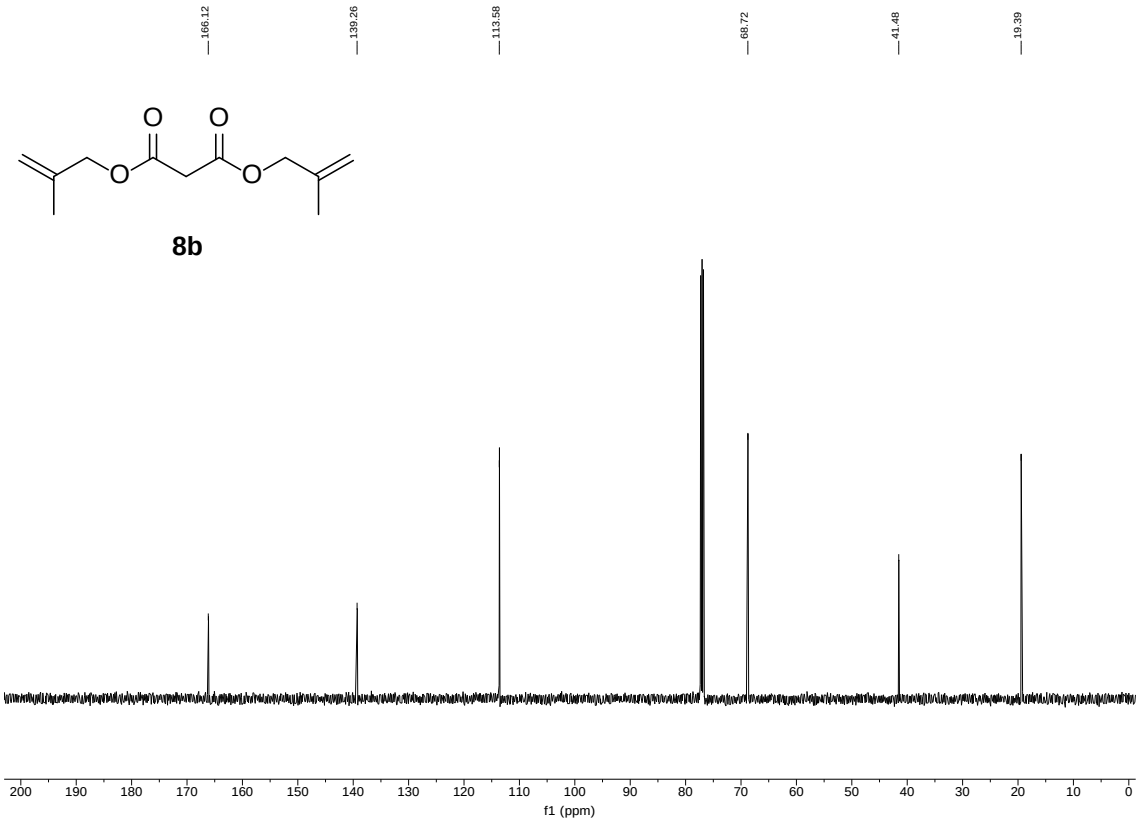
4.04
1.99
6.14
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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68.72
41.48
19.39
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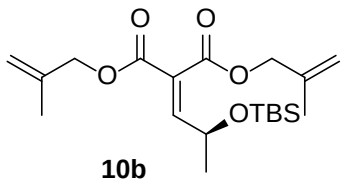
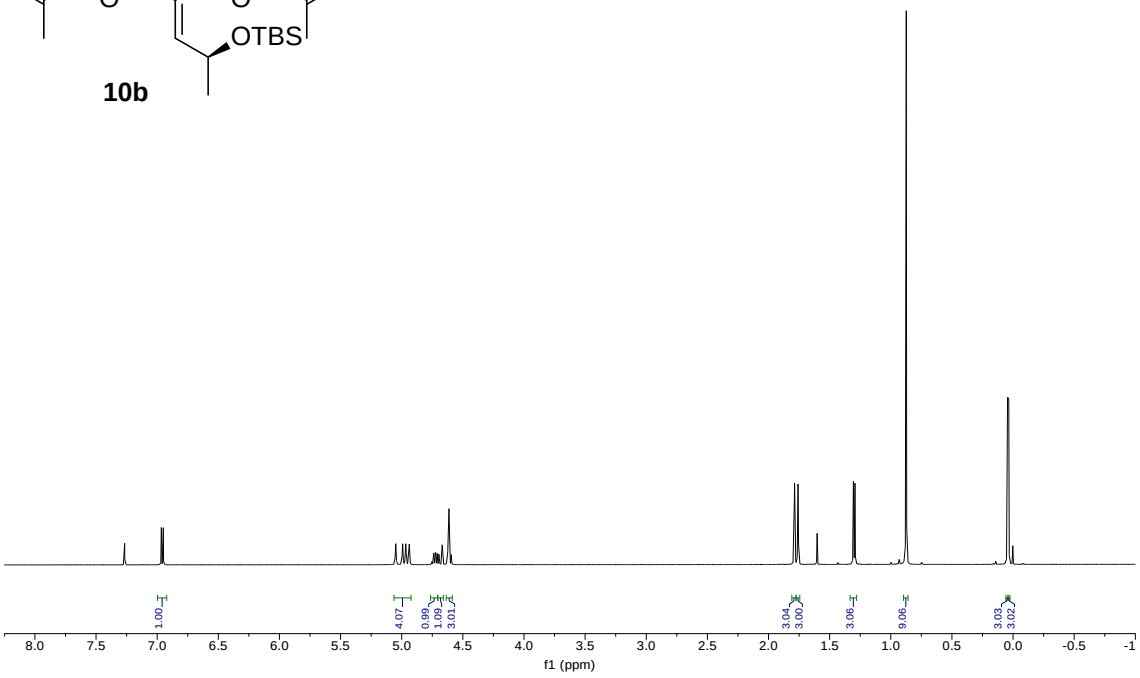
f1 (ppm)

8b


O
O
O
O
OTBS

10b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4.07
0.99
1.09
3.01
3.04
3.00
3.06
9.06
3.03
3.02
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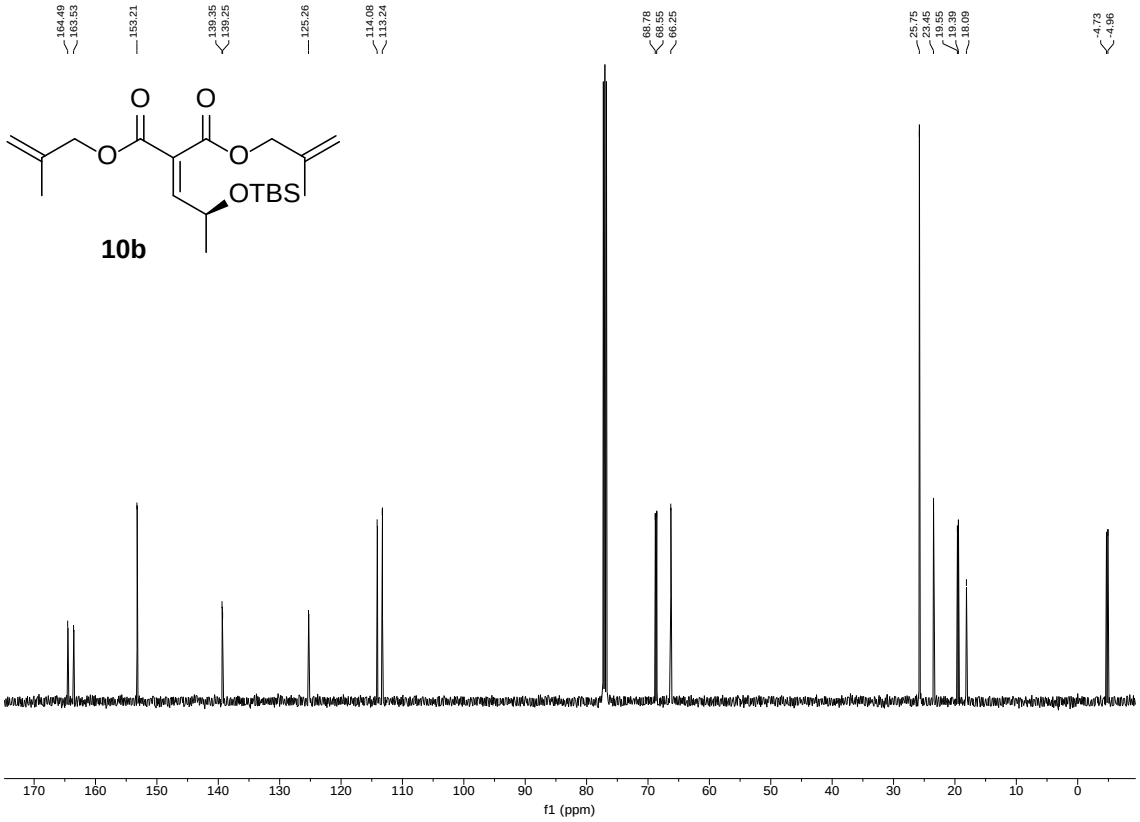
f1 (ppm)


164.49
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19.55
19.39
18.09
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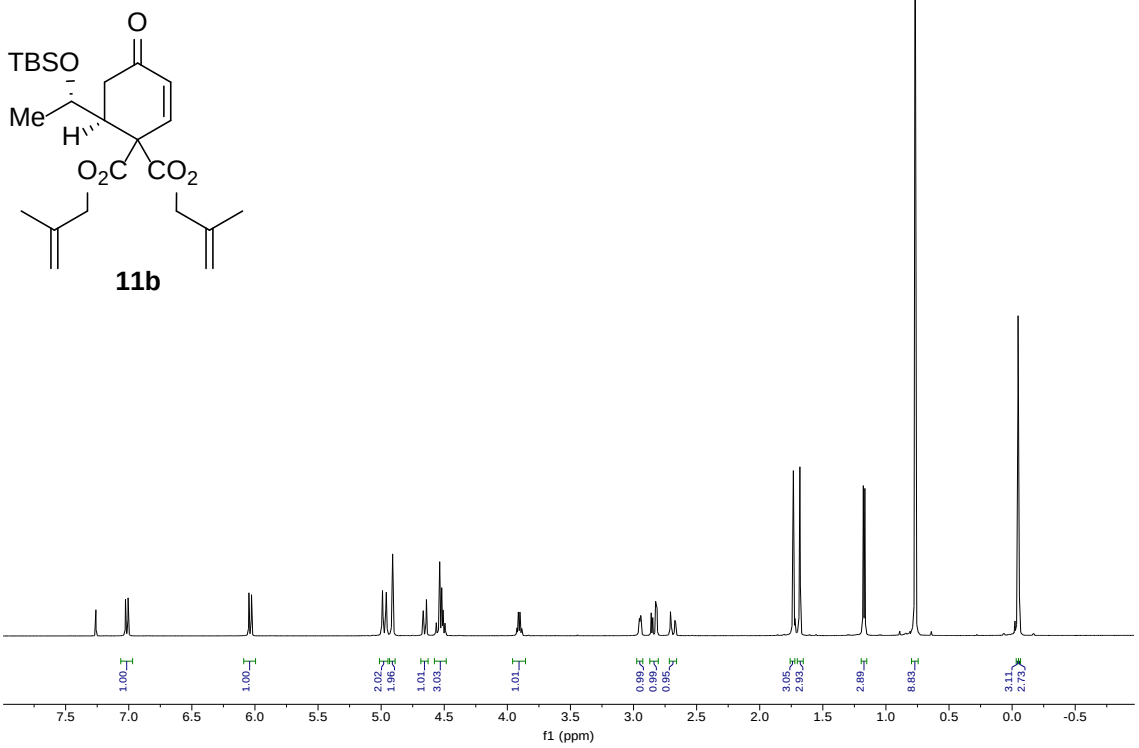
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

O
O
O
O
OTBS

10b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O
O2C
CO2
11b
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1.00
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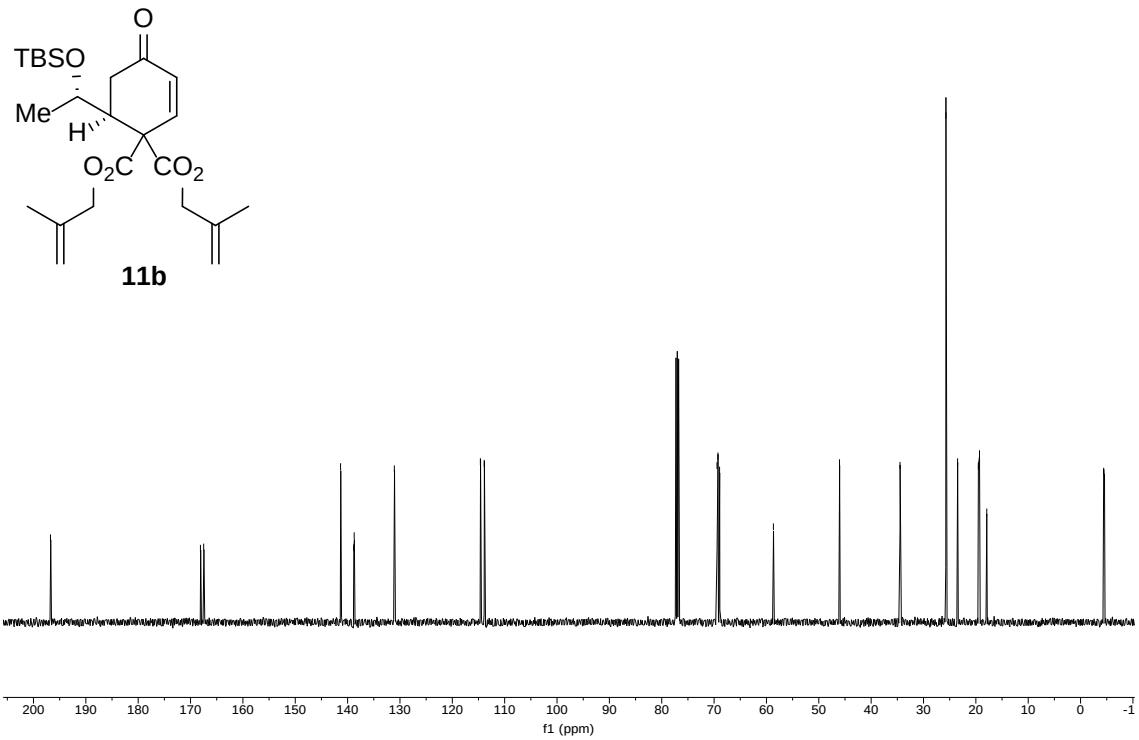
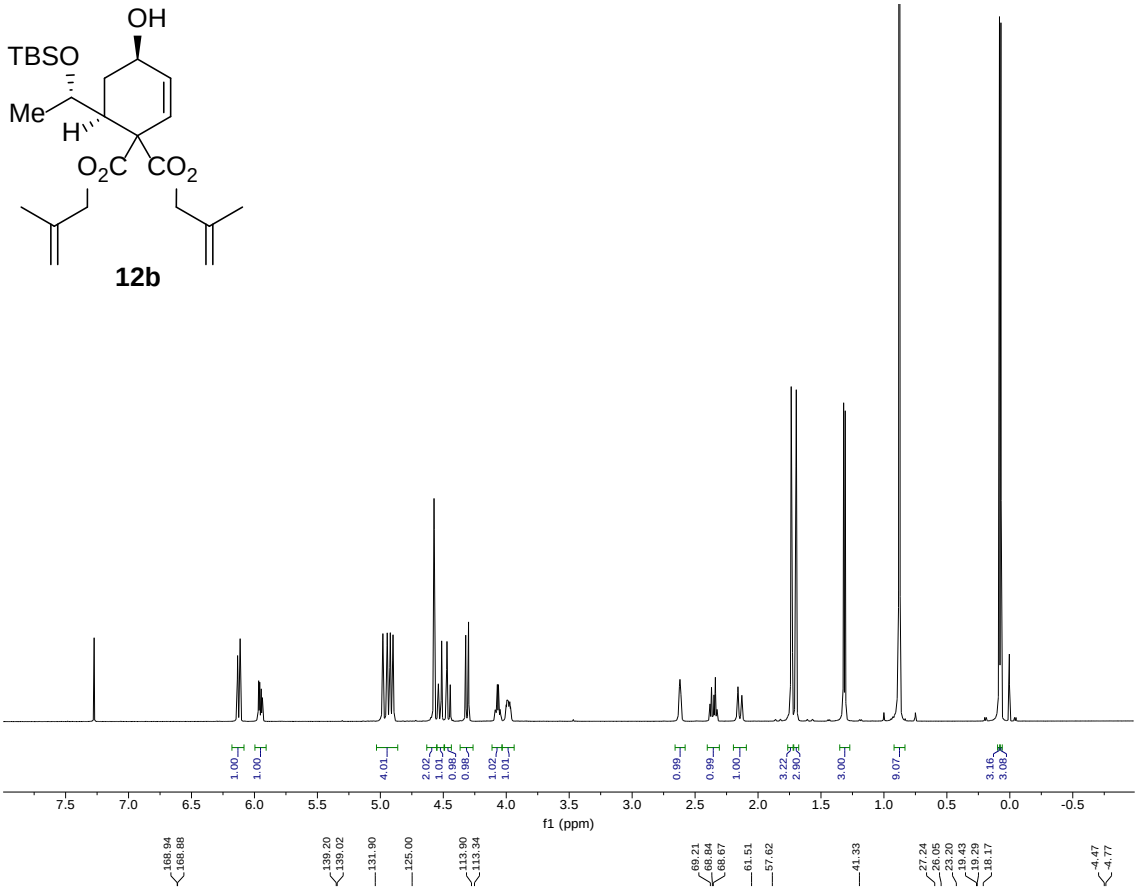
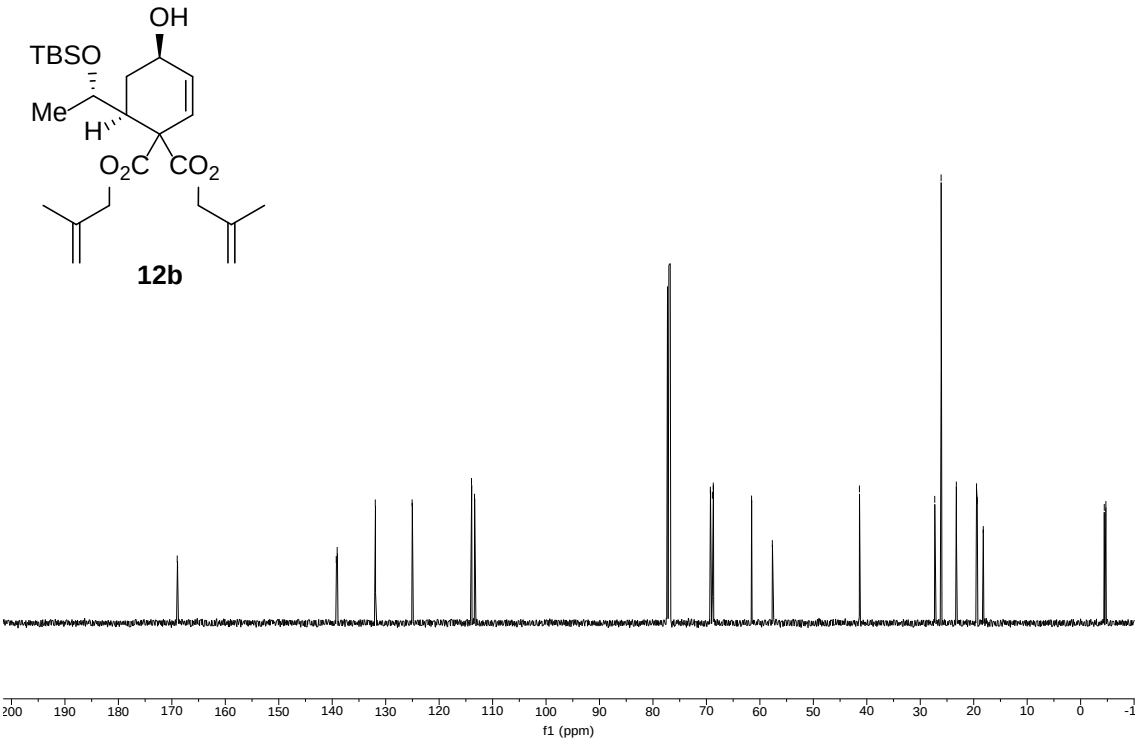
1.96
1.01
3.03
1.01
0.99
0.99
0.95
3.05
2.93
2.89
8.83
3.11
2.73
f1 (ppm)
196.71
168.06
167.44
141.29
138.80
138.69
131.02
114.59
113.86
69.39
69.22
68.90
58.62
45.99
34.43
25.68
23.44
19.47
19.26
17.87
-4.47
-4.63

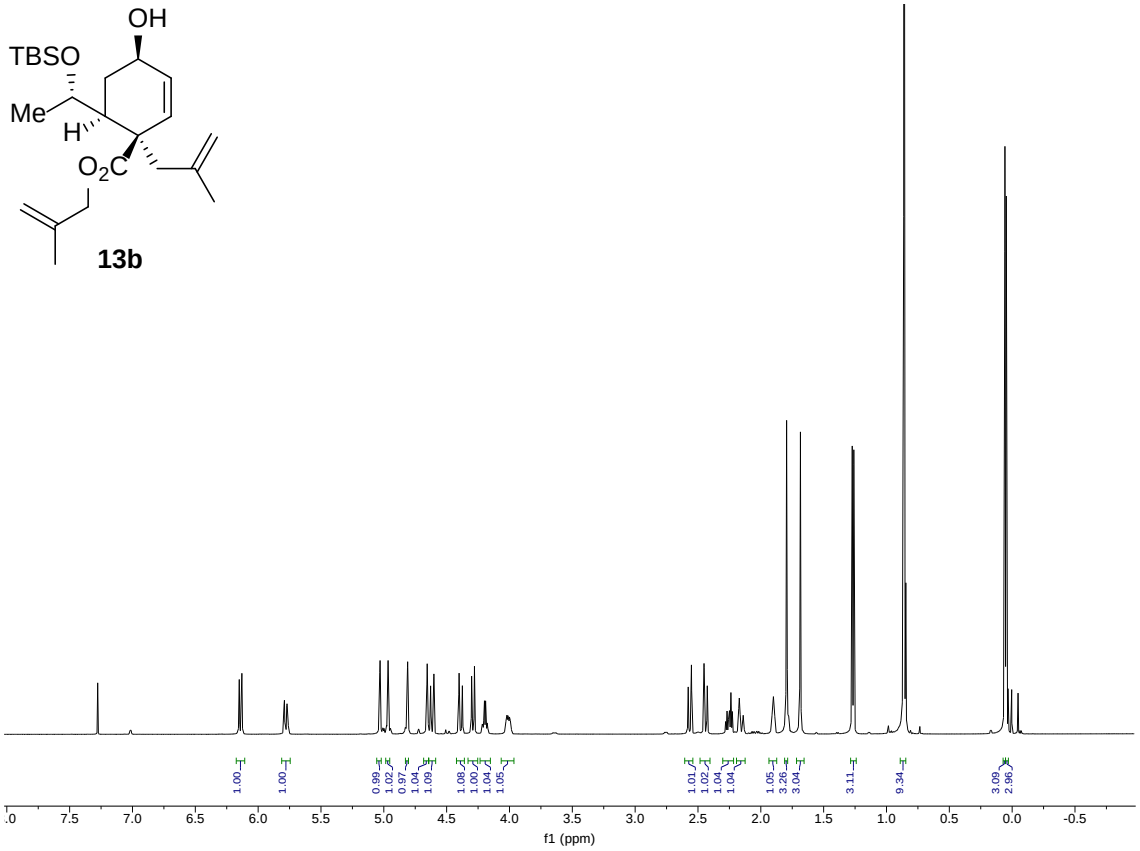

TBSO
Me
H
O
O2C
CO2
11b
f1 (ppm)

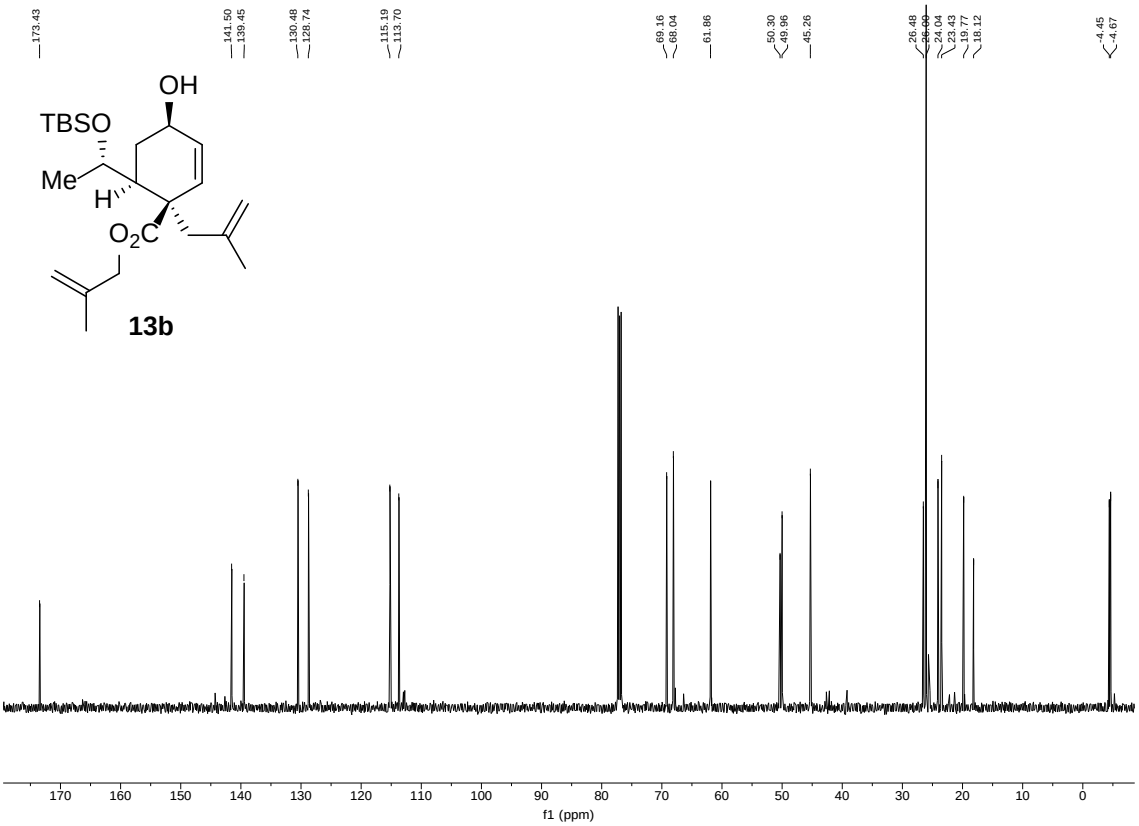

OH
TBSO
Me
H
O2C
CO2
12b
1.00
1.00
4.01
2.02
1.01
0.98
0.98
1.02
1.01
0.99
0.99
1.00
3.22
2.90
3.00
9.07
3.16
3.08
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
166.94
166.88
139.20
139.02
131.90
125.00
113.90
113.34
69.21
68.84
68.67
61.51
57.62
41.33
27.24
26.05
23.20
19.43
19.29
18.17
-4.47
-4.77


OH
TBSO
Me
H
O2C
CO2
12b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

OH
TBSO
Me
H
O2C

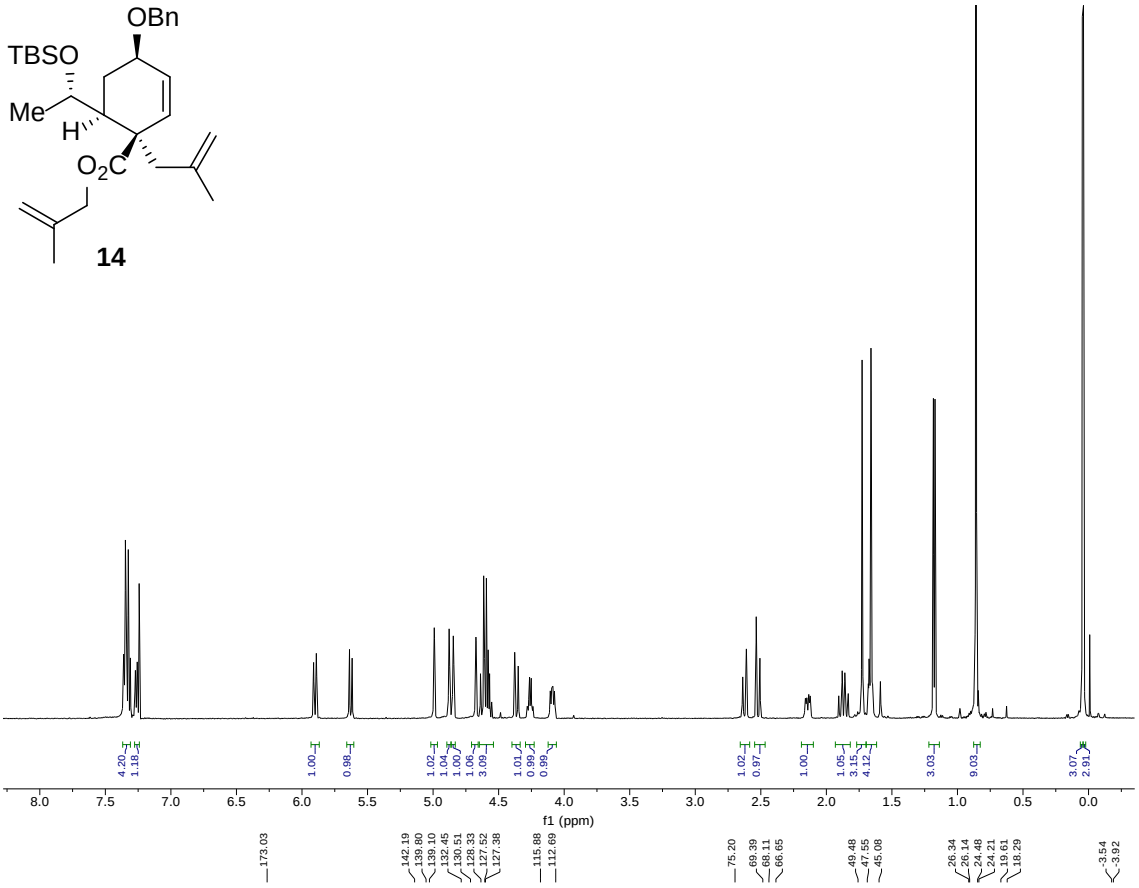
13b

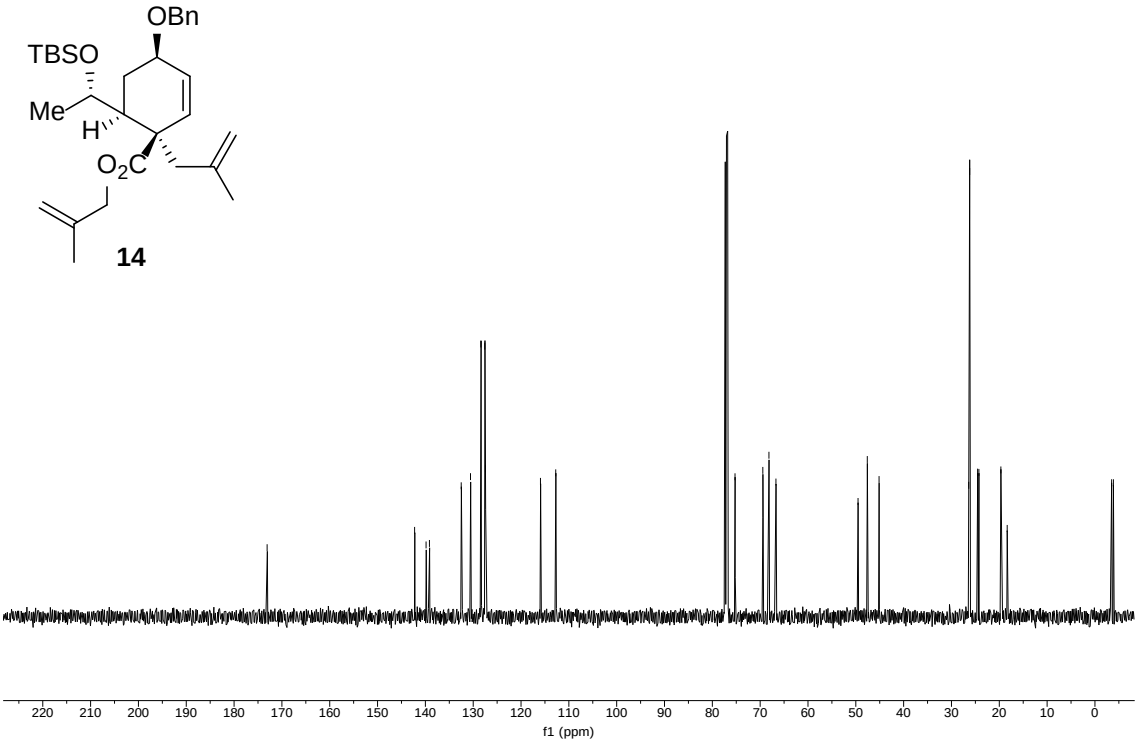

1.00
1.00
0.99
1.02
0.97
1.04
1.09
1.08
1.00
1.04
1.05
1.01
1.02
1.04
1.04
1.05
3.26
3.04
3.11
9.34
3.09
2.96
f1 (ppm)


173.43
141.50
139.45
130.48
128.74
115.19
113.70
69.16
68.04
61.86
50.30
49.96
45.26
26.48
26.00
24.04
23.43
19.77
18.12
-4.45
-4.67
f1 (ppm)

OH
TBSO
Me
H
O2C

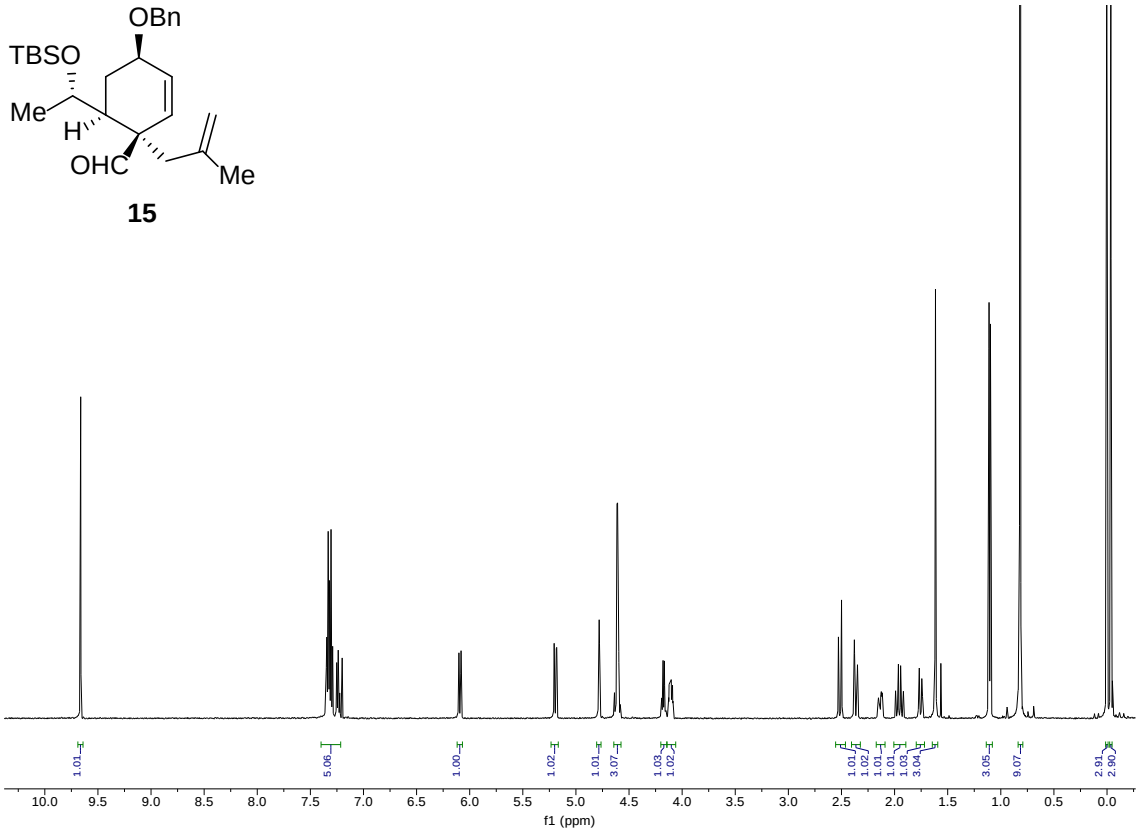
13b

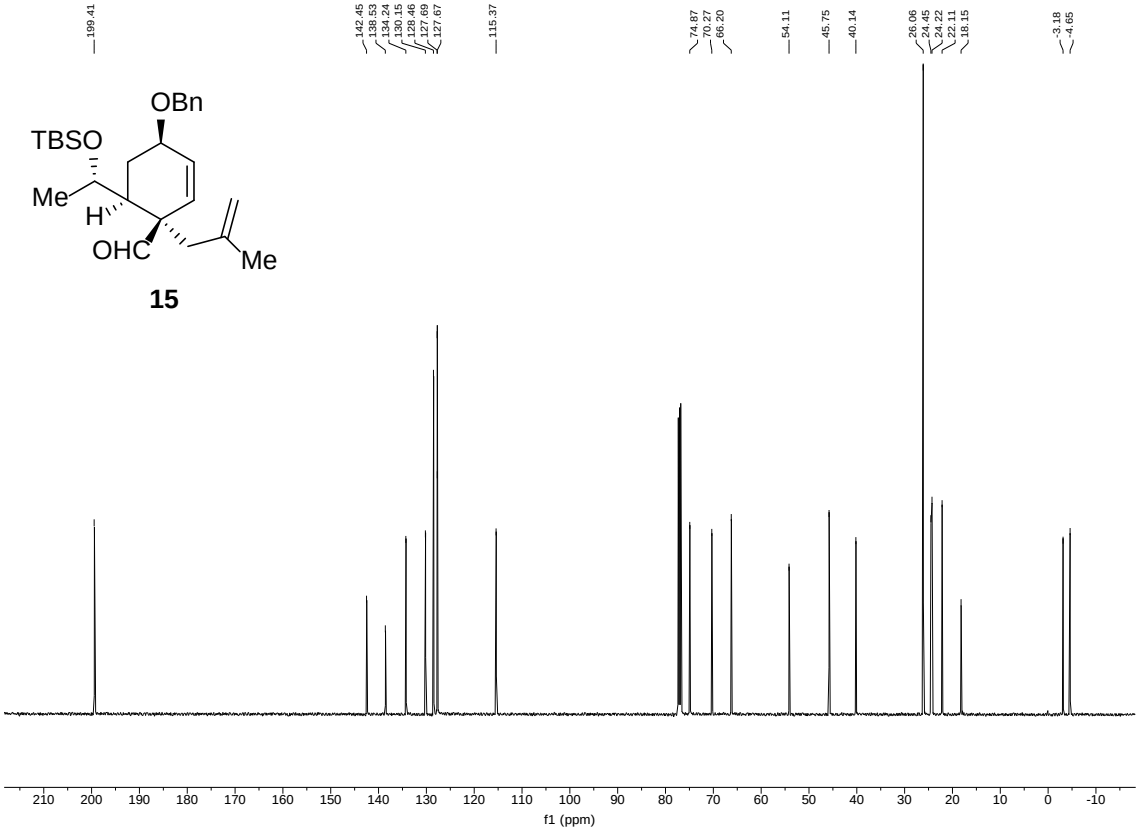

OBn
TBSO
Me
H
O2C
14
4.20
1.18
1.00
0.98
1.02
1.04
1.00
1.06
3.09
1.01
0.99
0.99
1.02
0.97
1.00
1.05
3.15
4.12
3.03
9.03
3.07
2.91
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
173.03
142.19
139.80
139.10
132.45
130.51
128.33
127.52
127.38
115.88
112.69
75.20
69.39
68.11
66.65
49.48
47.55
45.08
26.34
26.14
24.48
24.21
19.61
18.29
-3.54
-3.92


OBn
TBSO
Me
H
O2C
14
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

OBn
TBSO
Me
H
OHC
Me

15

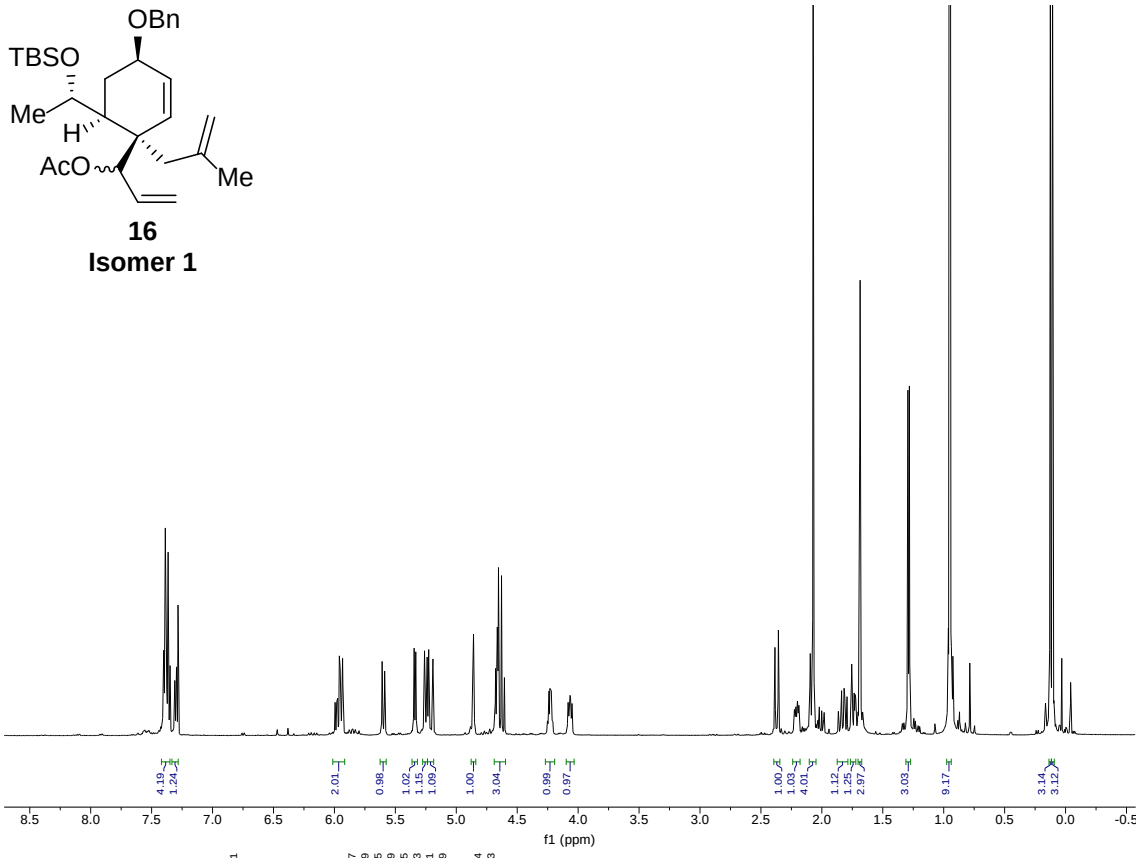

1.01
5.06
1.00
1.02
1.01
3.07
1.03
1.02
1.01
1.02
1.01
1.01
1.03
3.04
3.05
9.07
2.91
2.90
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


199.41
142.45
138.53
134.24
130.15
128.46
127.69
127.67
115.37
74.87
70.27
66.20
54.11
45.75
40.14
26.06
24.45
24.22
22.11
18.15
-3.18
-4.65
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

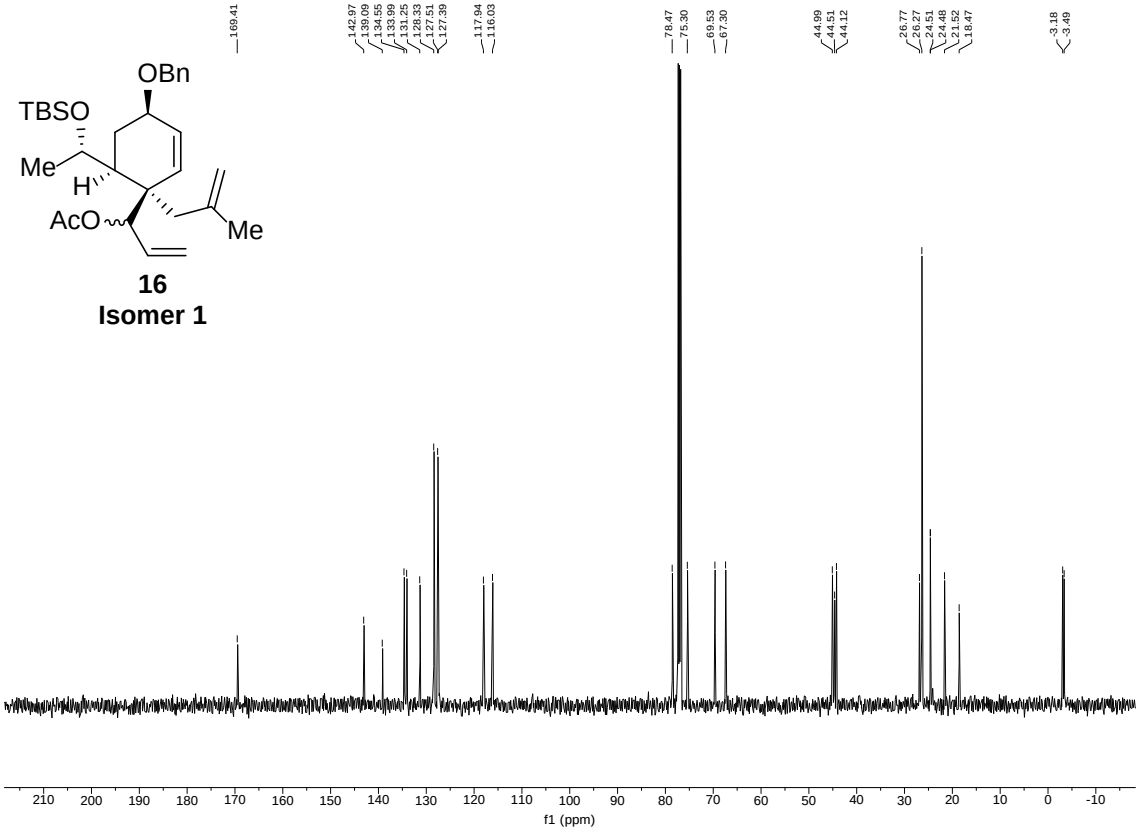
OBn
TBSO
Me
H
OHC
Me

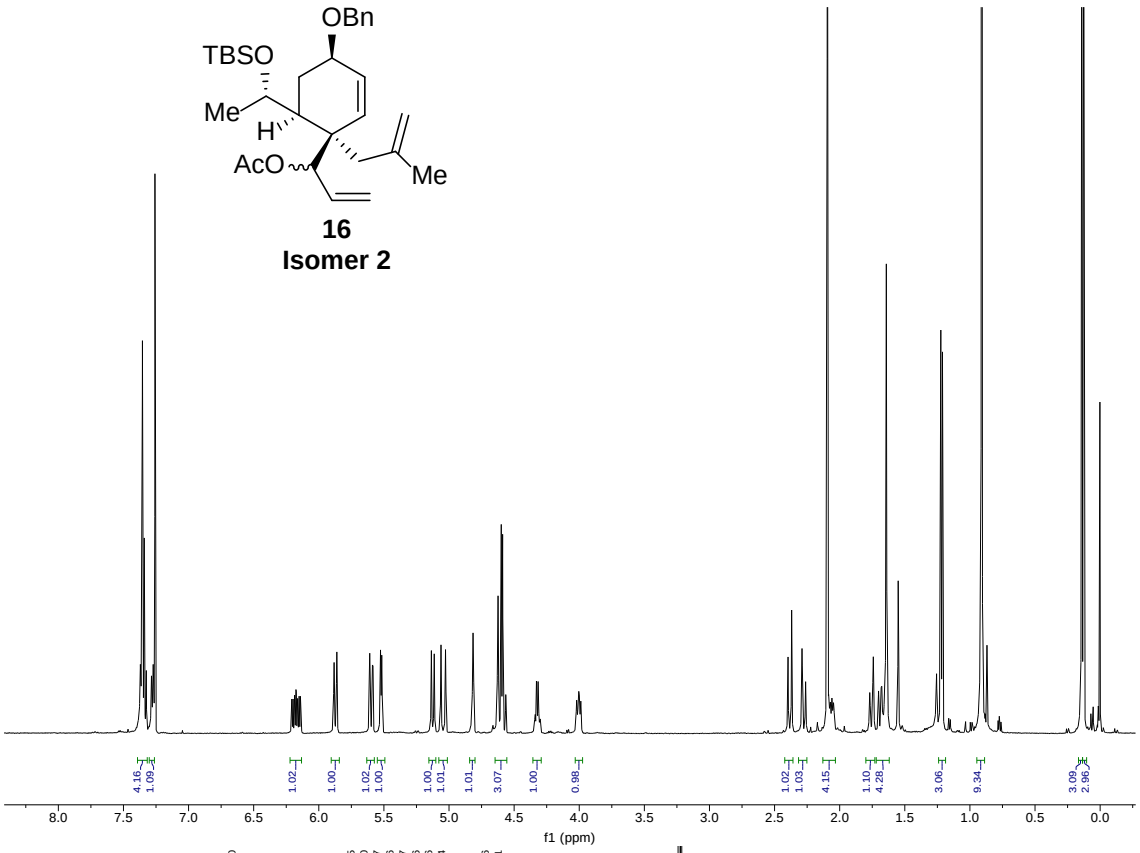
15

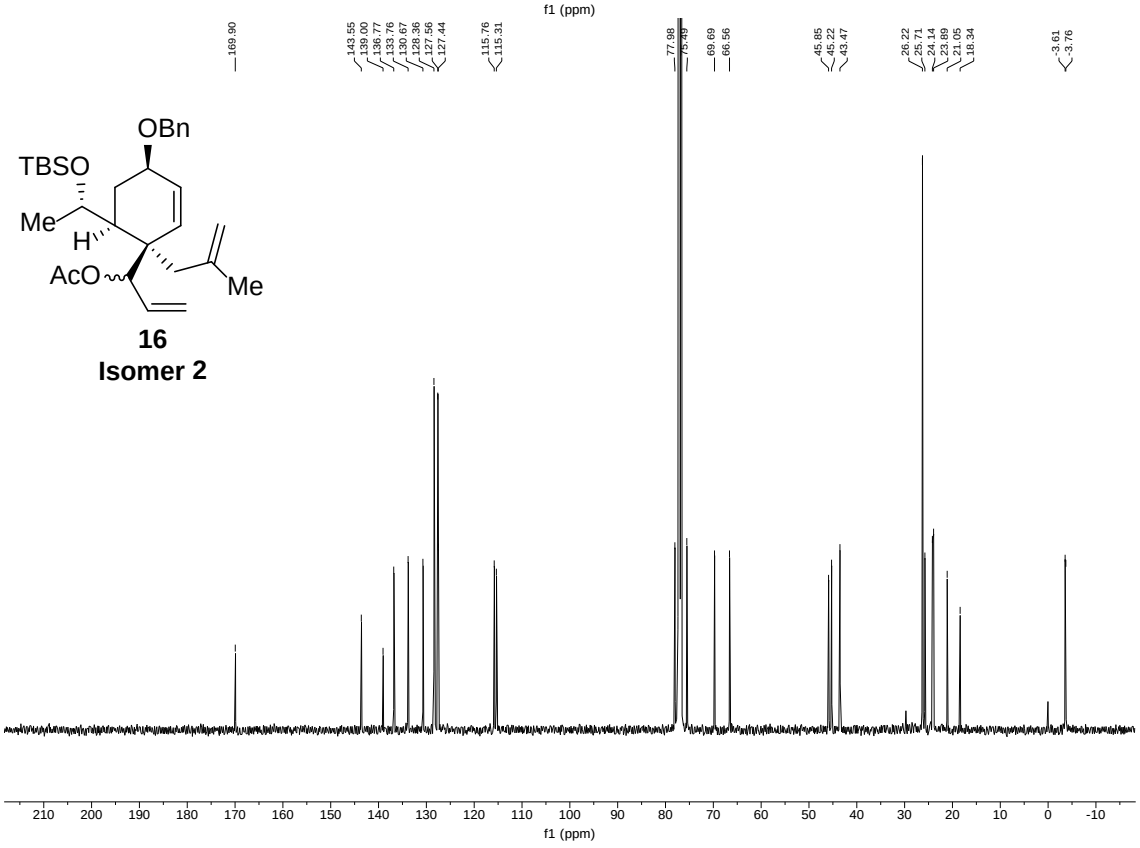
16
Isomer 1

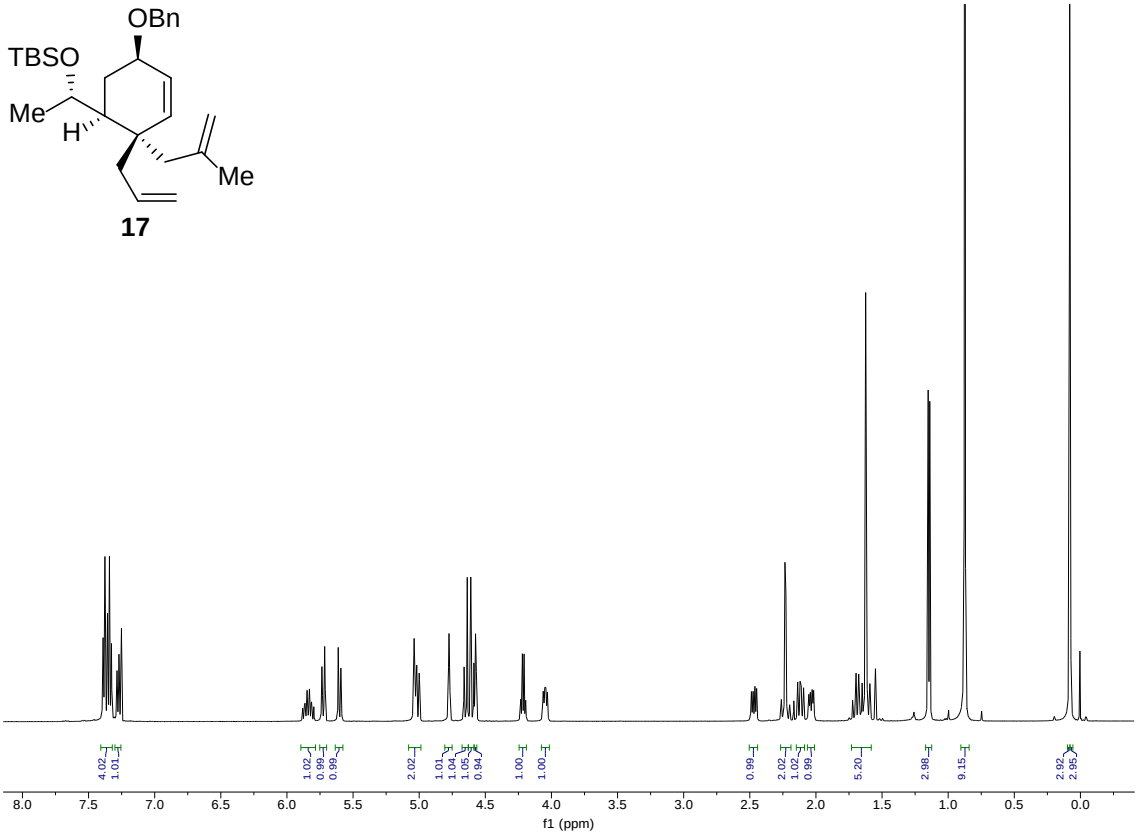


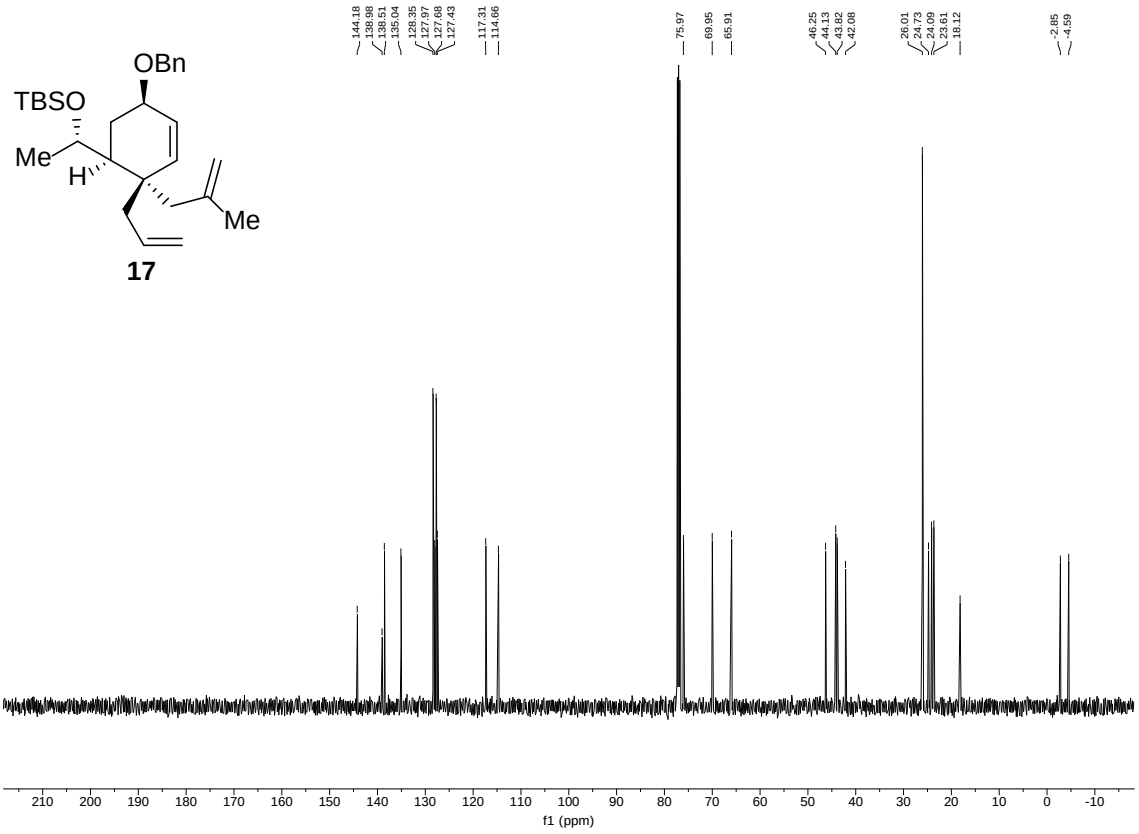
16
Isomer 1




OBn
TBSO
Me
H
AcO
Me
16
Isomer 2
4.16
1.09
1.02
1.00
1.02
1.00
1.00
1.01
1.01
3.07
1.00
0.98
1.02
1.03
4.15
1.10
4.29
3.06
9.34
3.09
2.96
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

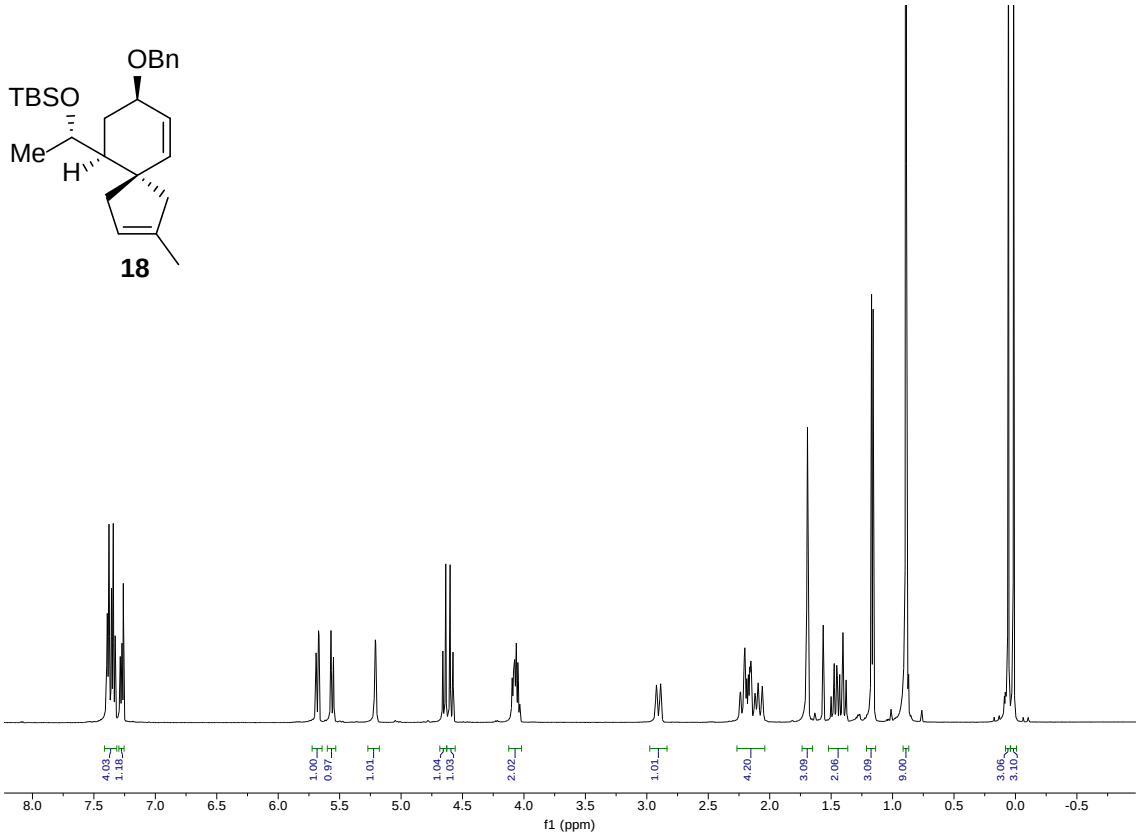

169.90
143.55
139.00
136.77
133.76
130.67
128.36
127.56
127.44
115.76
115.31
77.98
75.49
69.69
66.56
45.85
45.22
43.47
26.22
25.71
24.14
23.89
21.05
18.34
-3.61
-3.76
OBn
TBSO
Me
H
AcO
Me
16
Isomer 2
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OBn
TBSO
Me
H
Me
17
4.02
1.01
1.02
0.99
0.99
2.02
1.01
1.04
1.05
0.94
1.00
1.00
0.99
2.02
1.02
0.99
5.20
2.98
9.15
2.92
2.95
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


144.18
138.98
138.51
135.04
128.35
127.97
127.68
127.43
117.31
114.66
75.97
69.95
65.91
46.25
44.13
43.82
42.08
26.01
24.73
24.09
23.61
18.12
-2.85
-4.59
OBn
TBSO
Me
H
Me
17
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

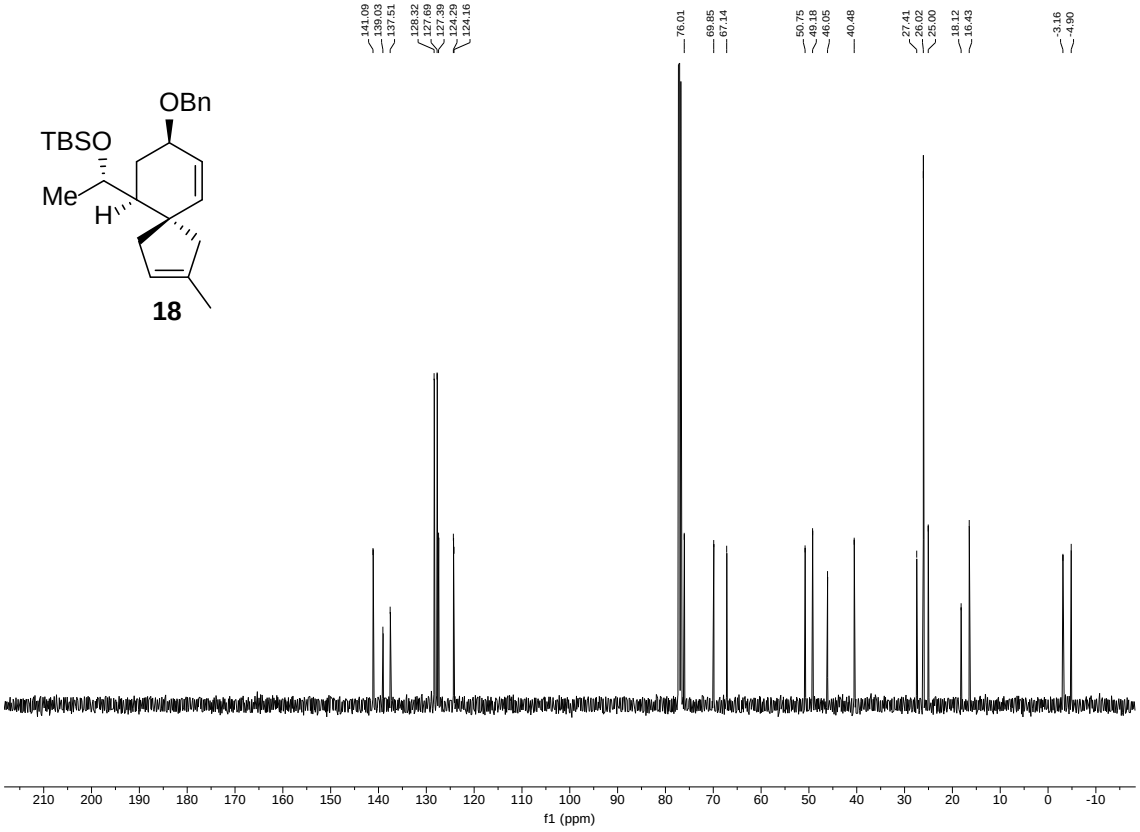
OBn
TBSO
Me
H

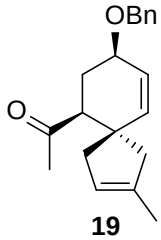
18


4.03
1.18
1.00
0.97
1.01
1.04
1.03
2.02
1.01
4.20
3.09
2.06
3.09
9.00
3.06
3.10
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

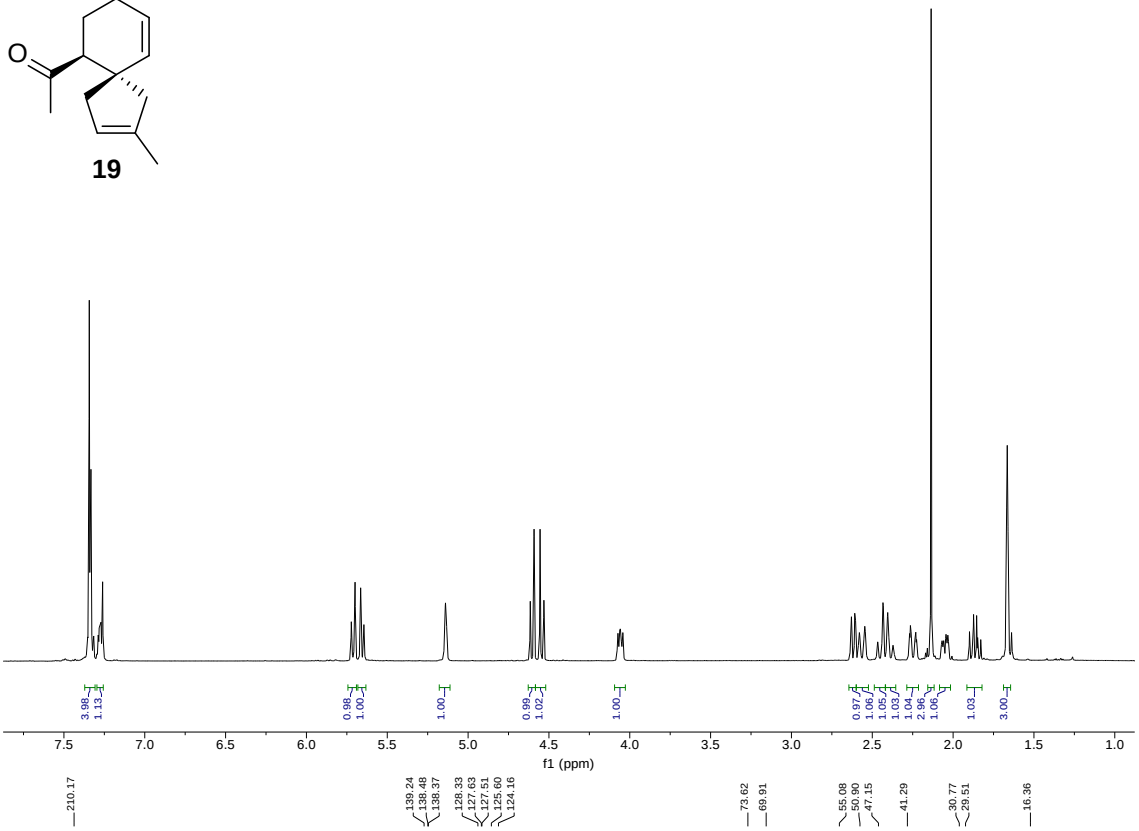
OBn
TBSO
Me
H

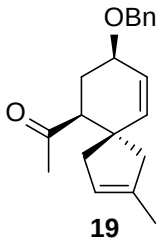
18


141.09
139.03
137.51
128.32
127.69
127.39
124.29
124.16
76.01
69.85
67.14
50.75
49.18
46.05
40.48
27.41
26.02
25.00
18.12
16.43
-3.16
-4.90
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

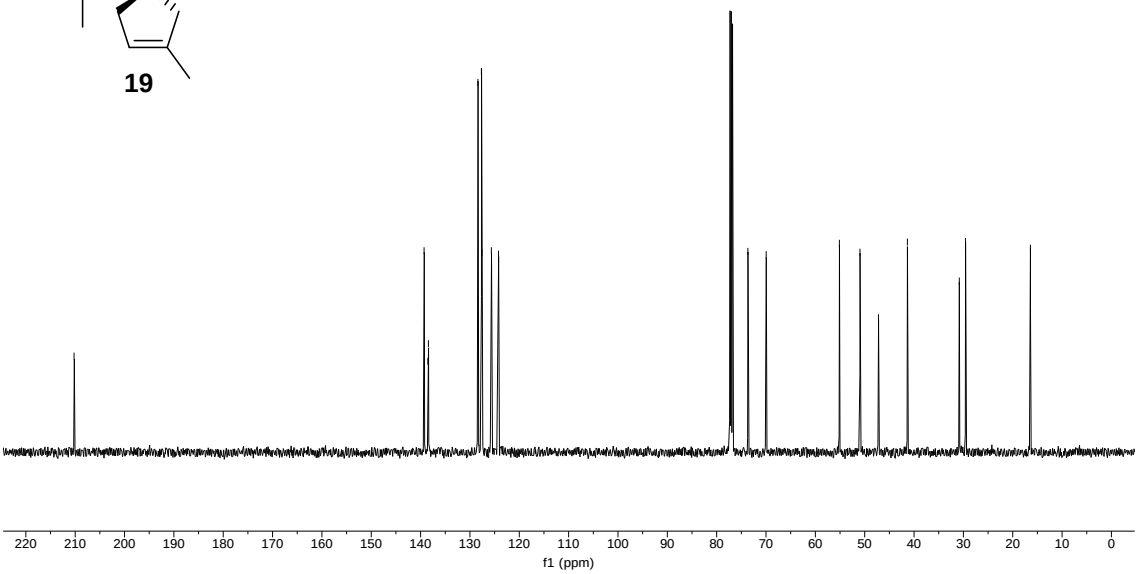

OBn
O

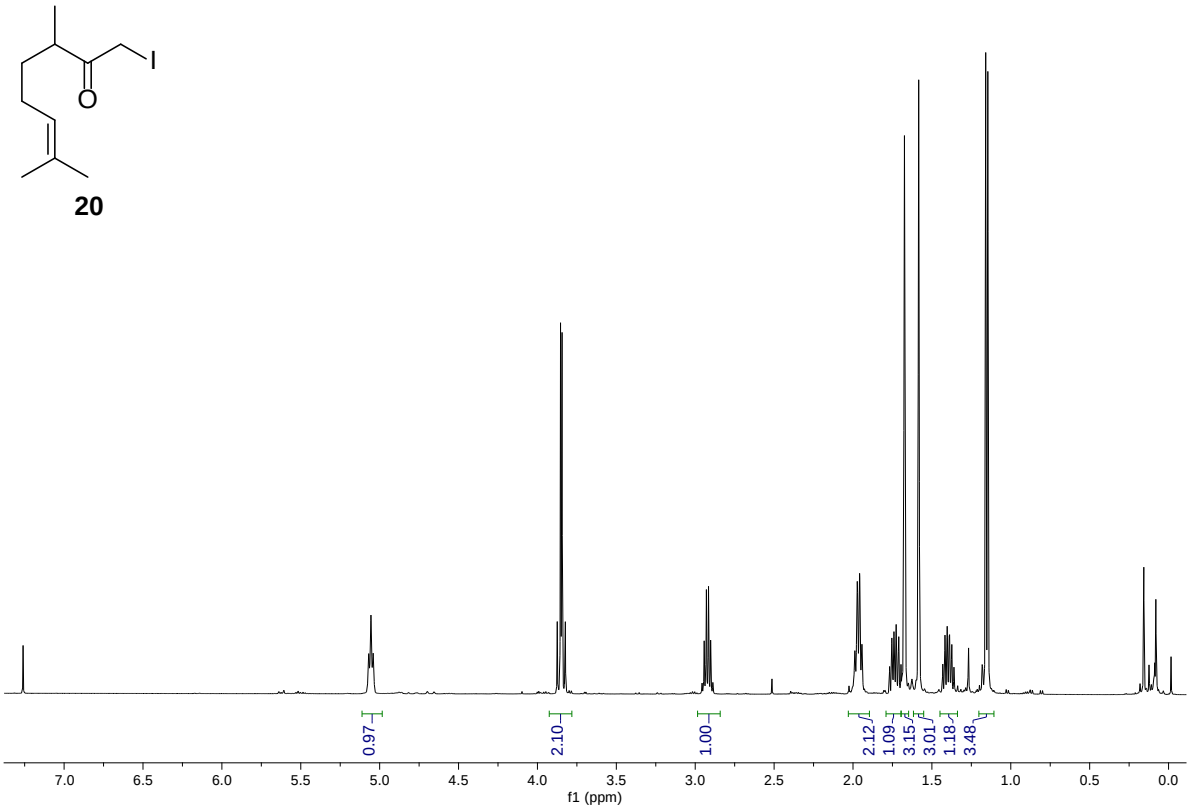
19

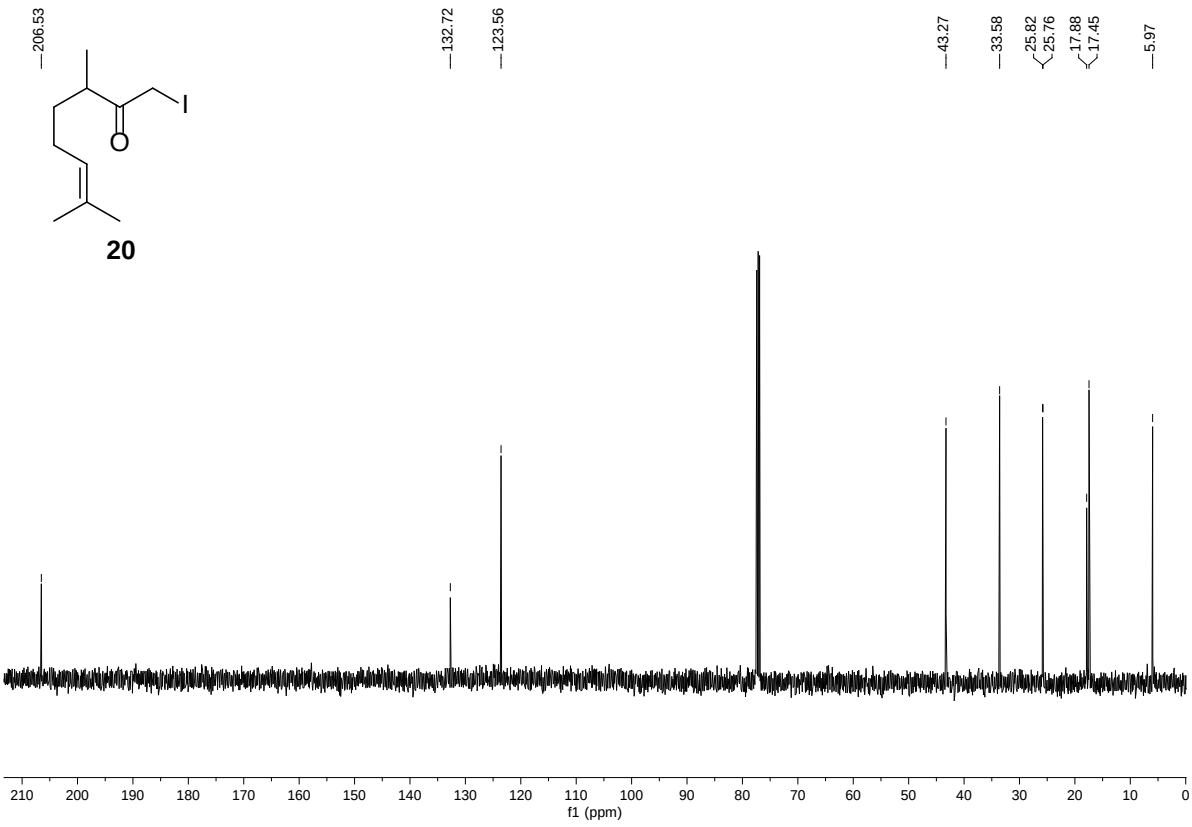

3.98
1.13
0.98
1.00
1.00
0.99
1.02
1.00
0.97
1.06
1.05
1.03
1.04
2.96
1.06
1.03
3.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)
210.17
139.24
138.48
138.37
128.33
127.63
127.51
125.60
124.16
73.62
69.91
55.08
50.90
47.15
41.29
30.77
29.51
16.36


OBn
O

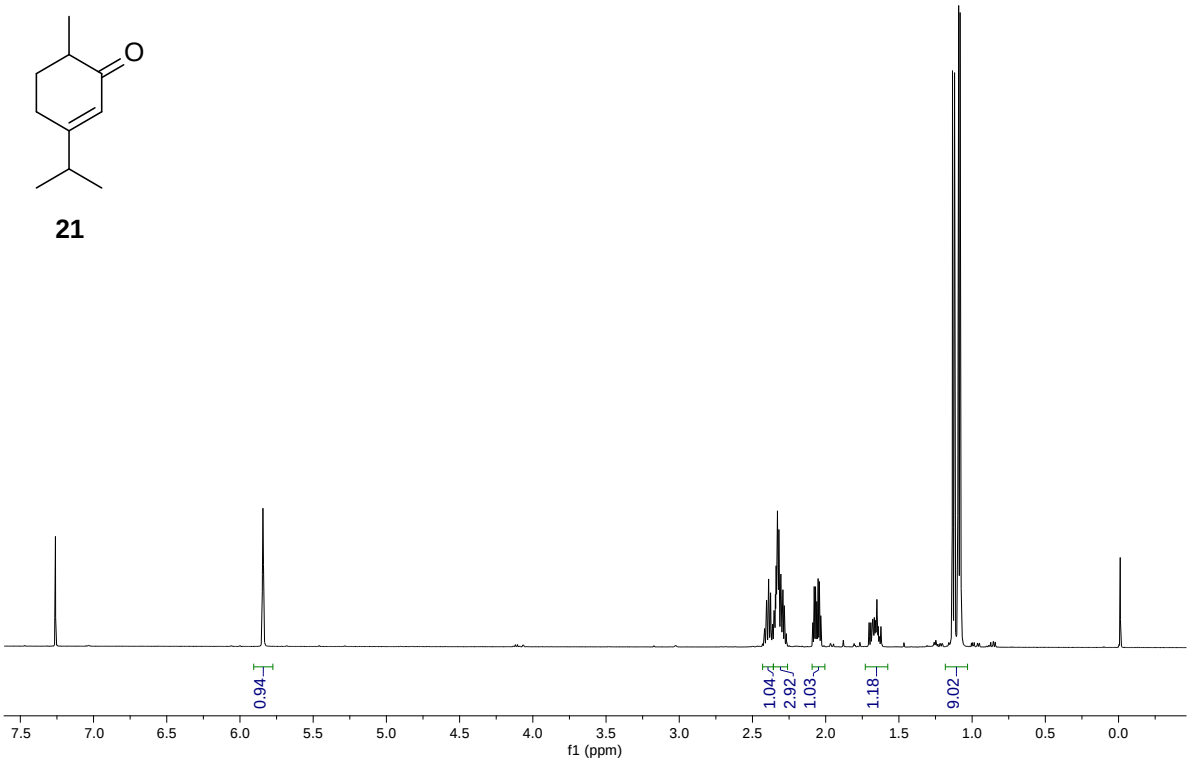
19


220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

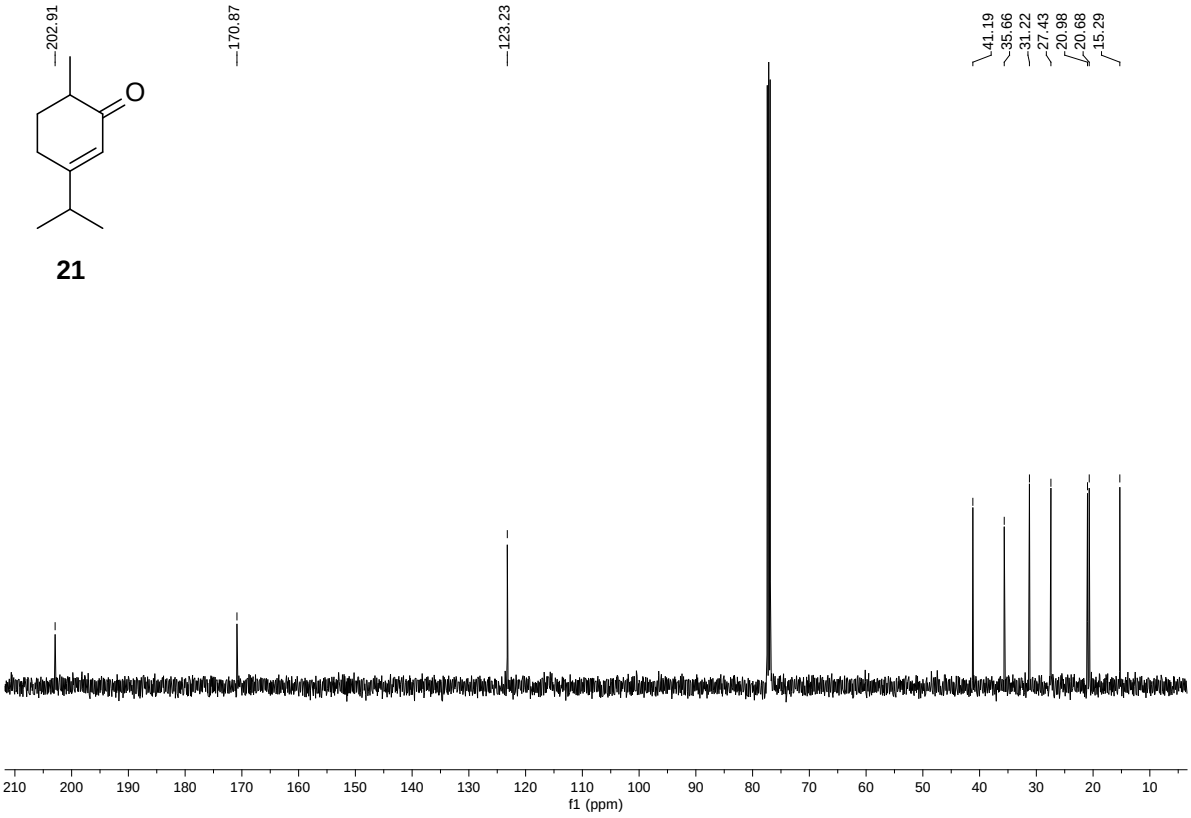

I
O
20
0.97
2.10
1.00
2.12
1.09
3.15
3.01
1.18
3.48
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

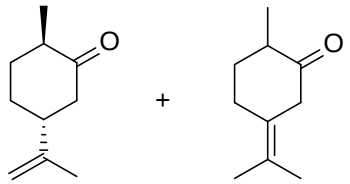

206.53
132.72
123.56
43.27
33.58
25.82
25.76
17.88
17.45
5.97
I
O
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

21

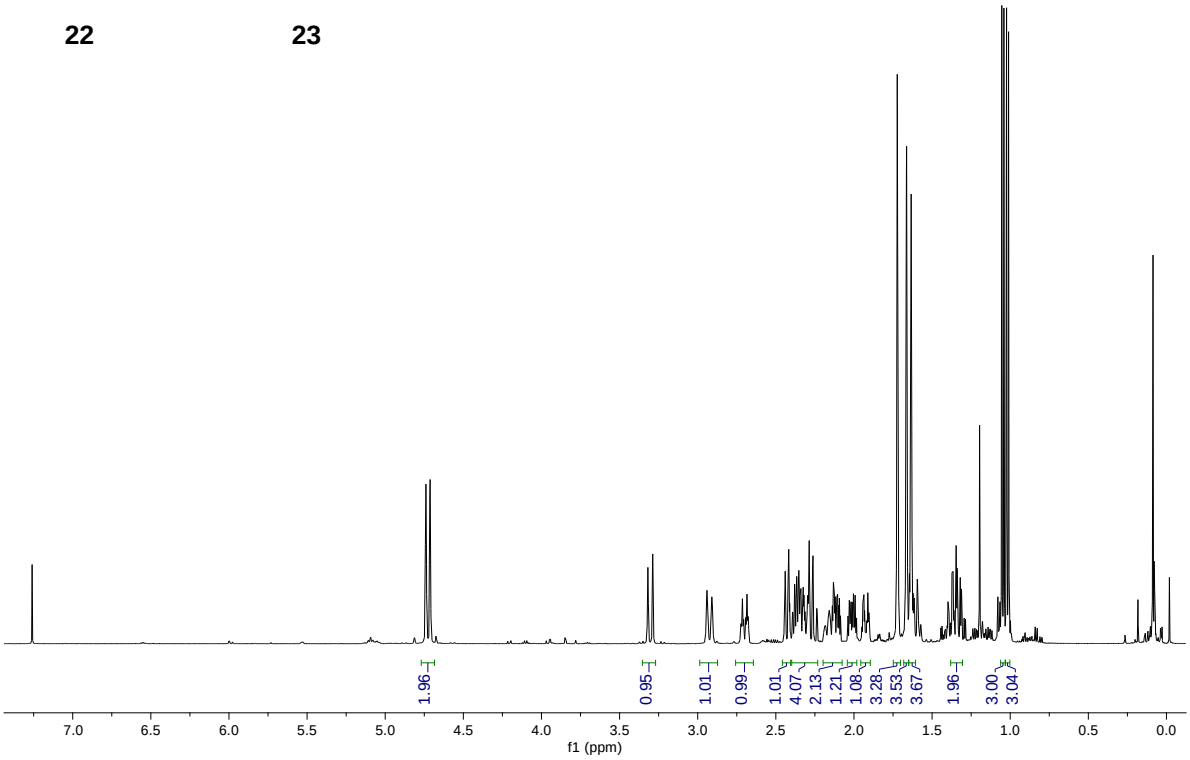

0.94
1.04
2.92
1.03
1.18
9.02
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

21

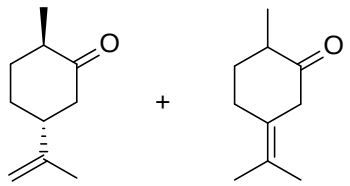

202.91
170.87
123.23
41.19
35.66
31.22
27.43
20.98
20.68
15.29
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



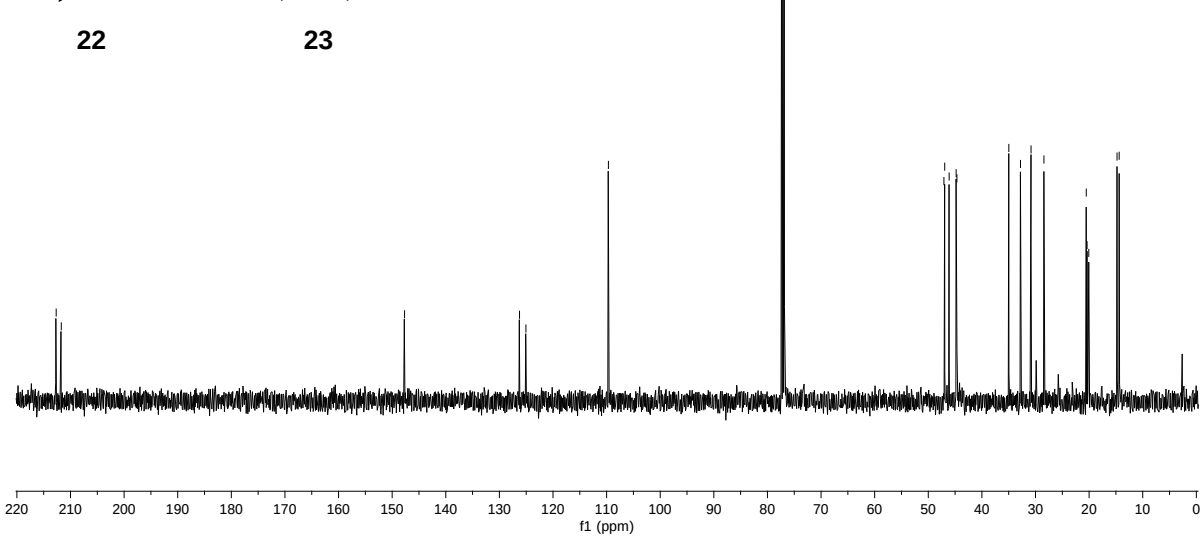
22 **23**

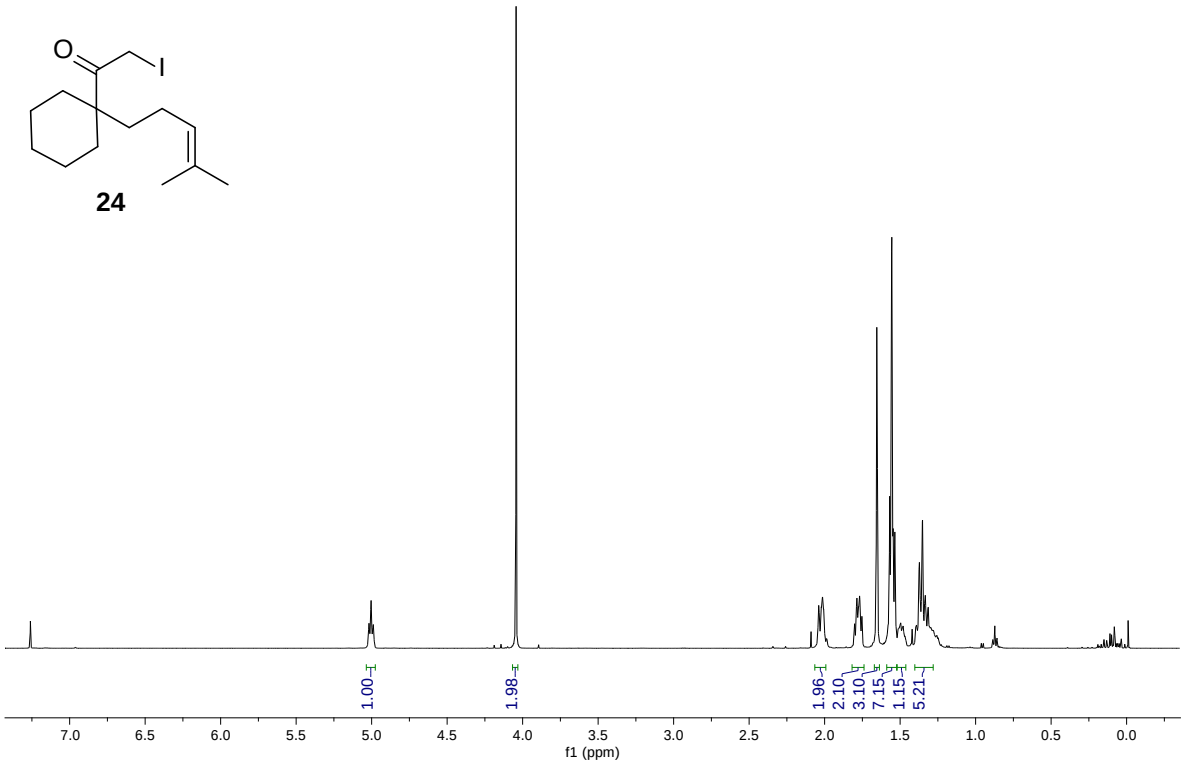

1.96
0.95
1.01
0.99
1.01
4.07
2.13
1.21
1.08
3.28
3.53
3.67
1.96
3.00
3.04
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

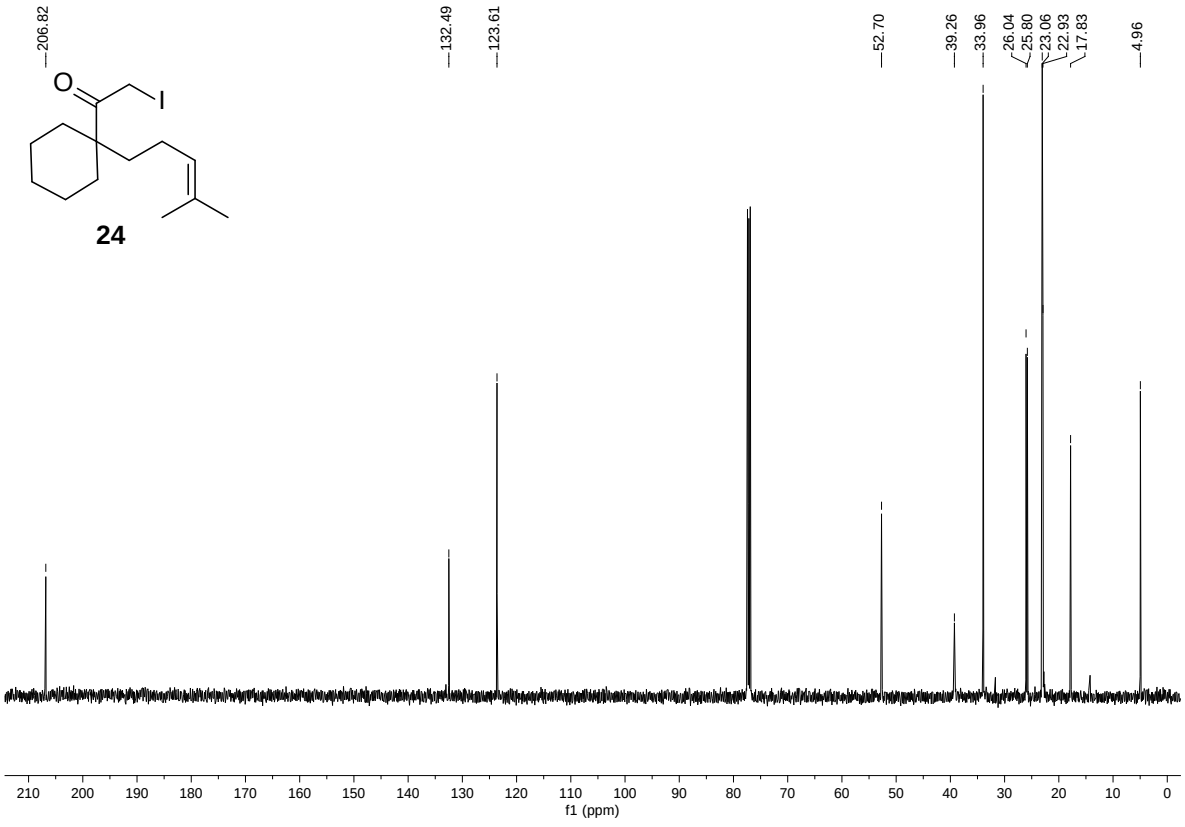

212.74
211.78
147.76
126.31
125.12
109.73
47.15
47.00
46.17
44.87
44.72
35.04
32.87
30.90
28.49
20.60
20.45
20.13
14.86
14.46

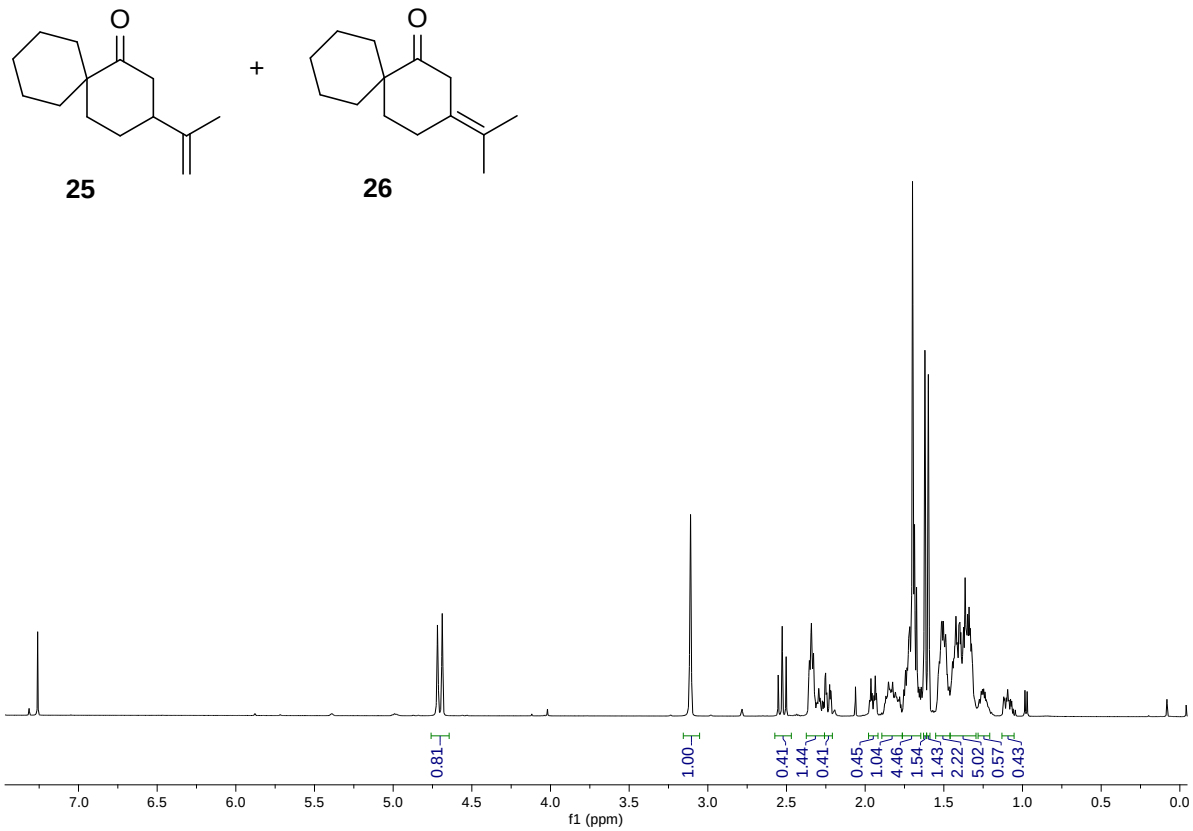


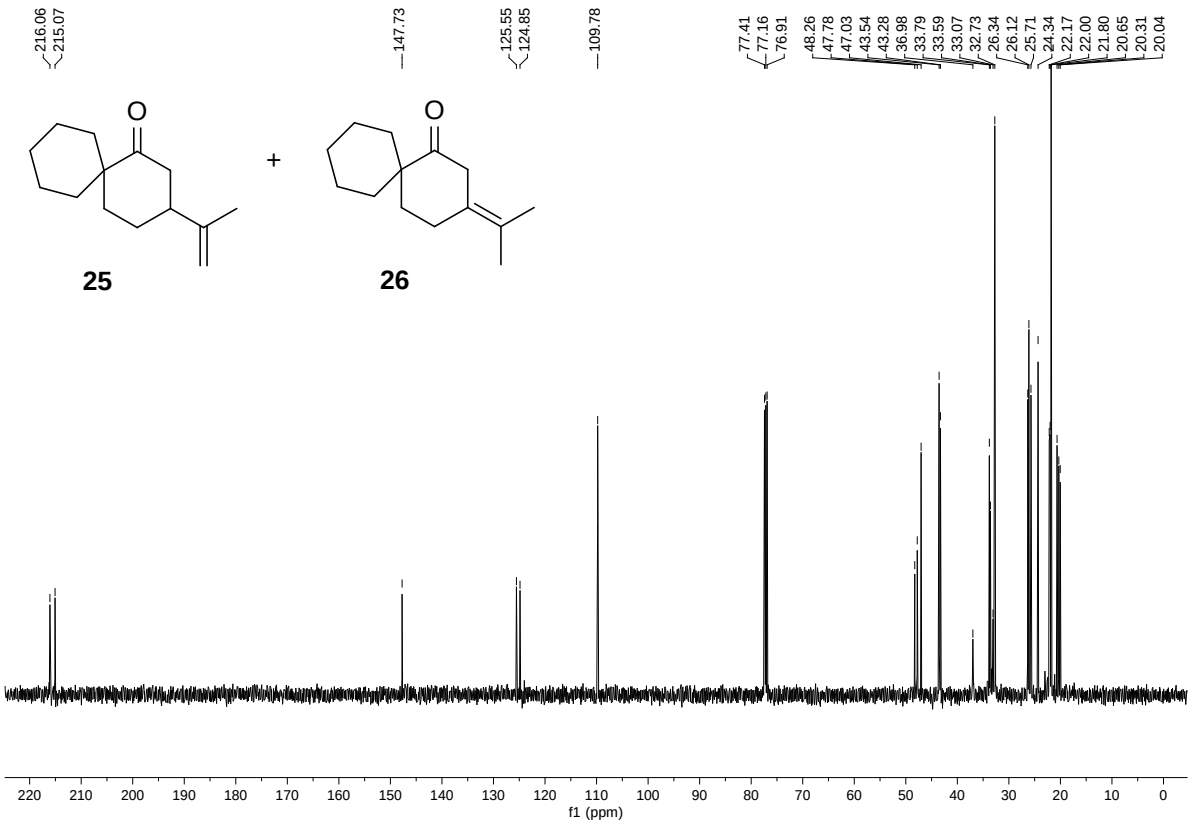
22 **23**

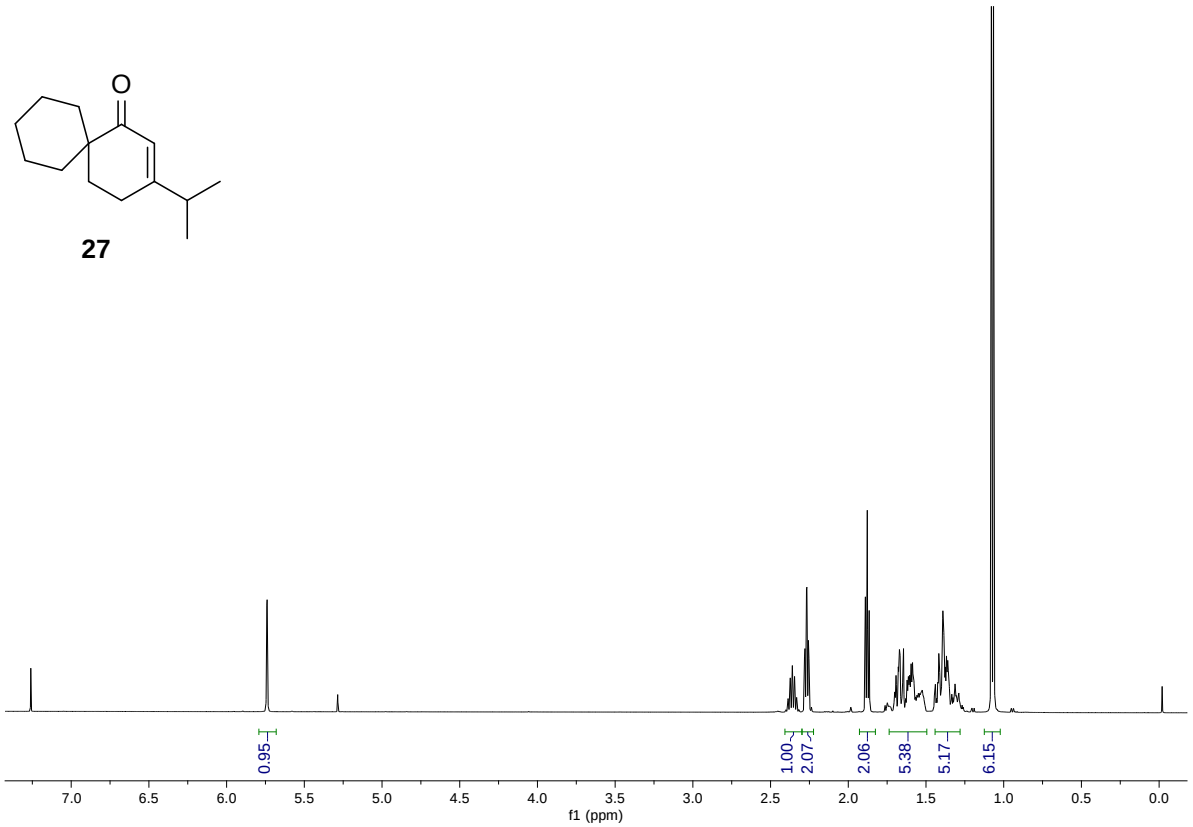

220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

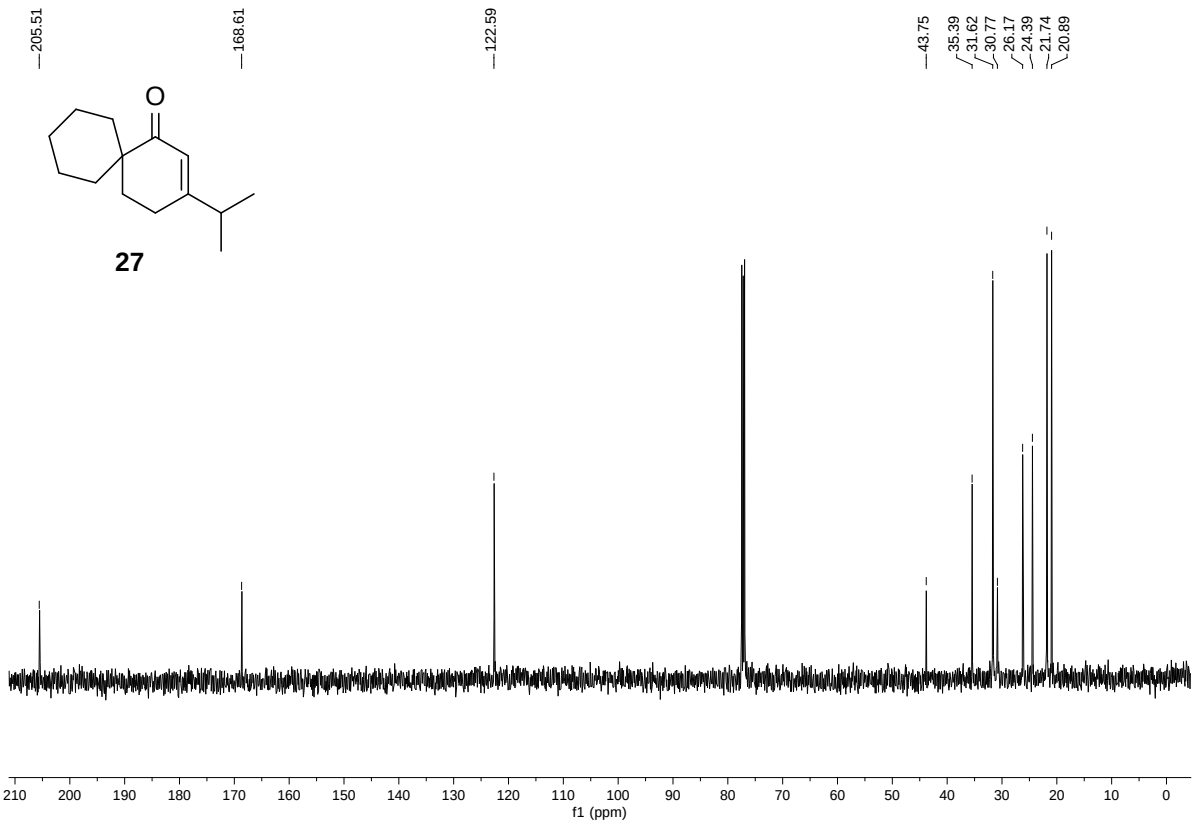

O
I
24
1.00
1.98
1.96
2.10
3.10
7.15
1.15
5.21
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

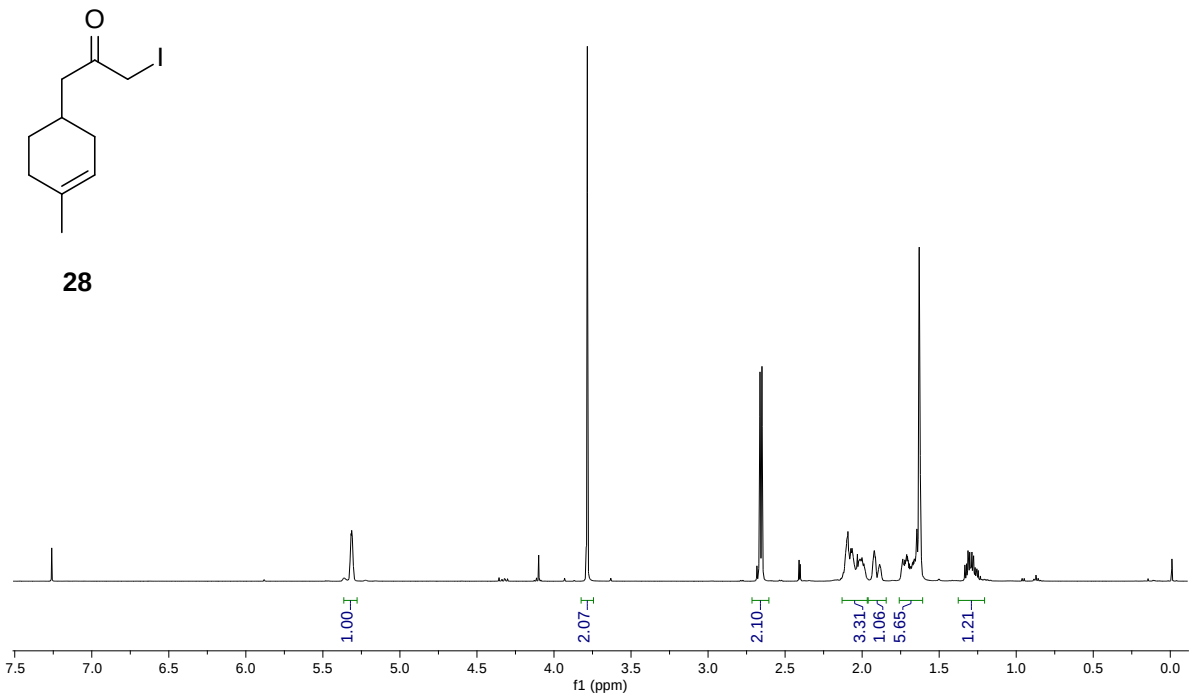

206.82
132.49
123.61
52.70
39.26
33.96
26.04
25.80
23.06
22.93
17.83
4.96
O
I
24
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

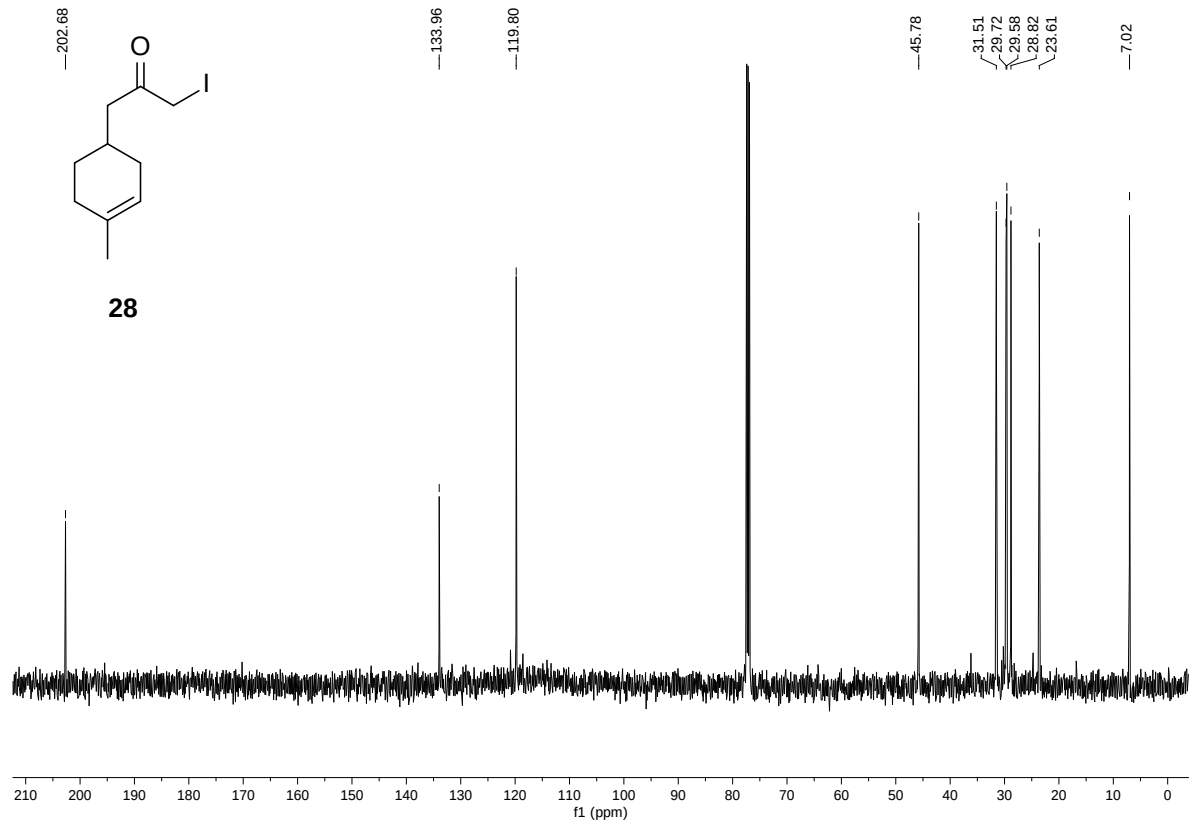

O
+
O
25
26
0.81
1.00
0.41
1.44
0.41
0.45
1.04
4.46
1.54
1.43
2.22
5.02
0.57
0.43
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

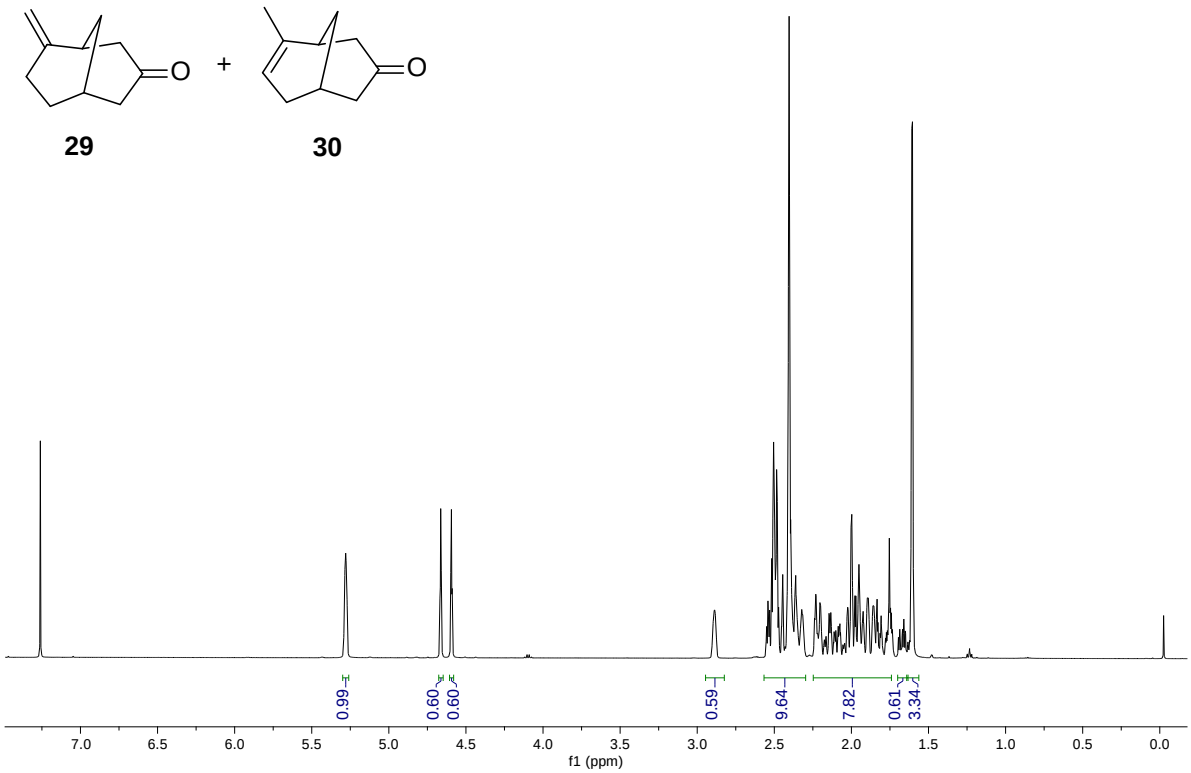

216.06
215.07
147.73
125.55
124.85
109.78
77.41
77.16
76.91
48.26
47.78
47.03
43.54
43.28
36.98
33.79
33.59
33.07
32.73
26.34
26.12
25.71
24.34
22.17
22.00
21.80
20.65
20.31
20.04
O
+
O
25
26
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

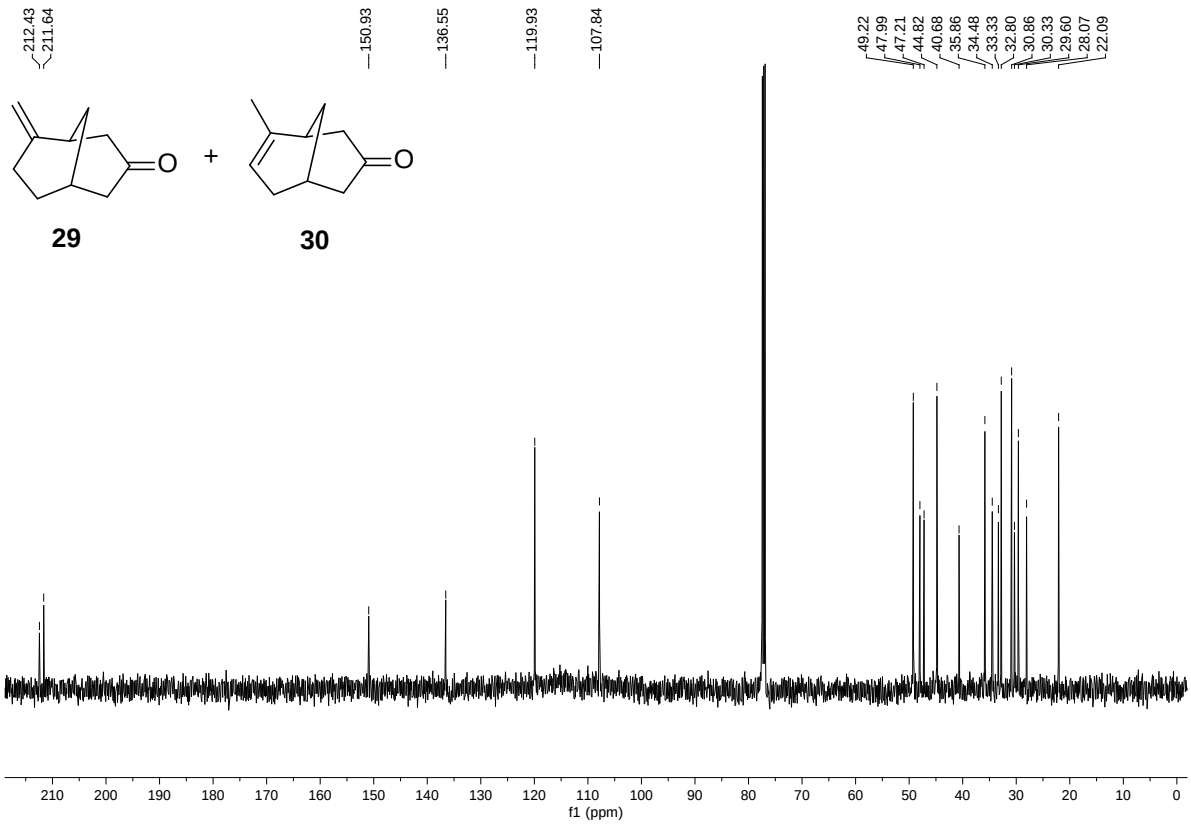

O
27
0.95
1.00
2.07
2.06
5.38
5.17
6.15
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

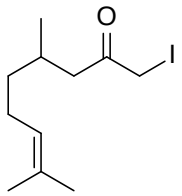

205.51
168.61
122.59
43.75
35.39
31.62
30.77
26.17
24.39
21.74
20.89
O
27
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
I
28
1.00
2.07
2.10
3.31
1.06
5.65
1.21
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

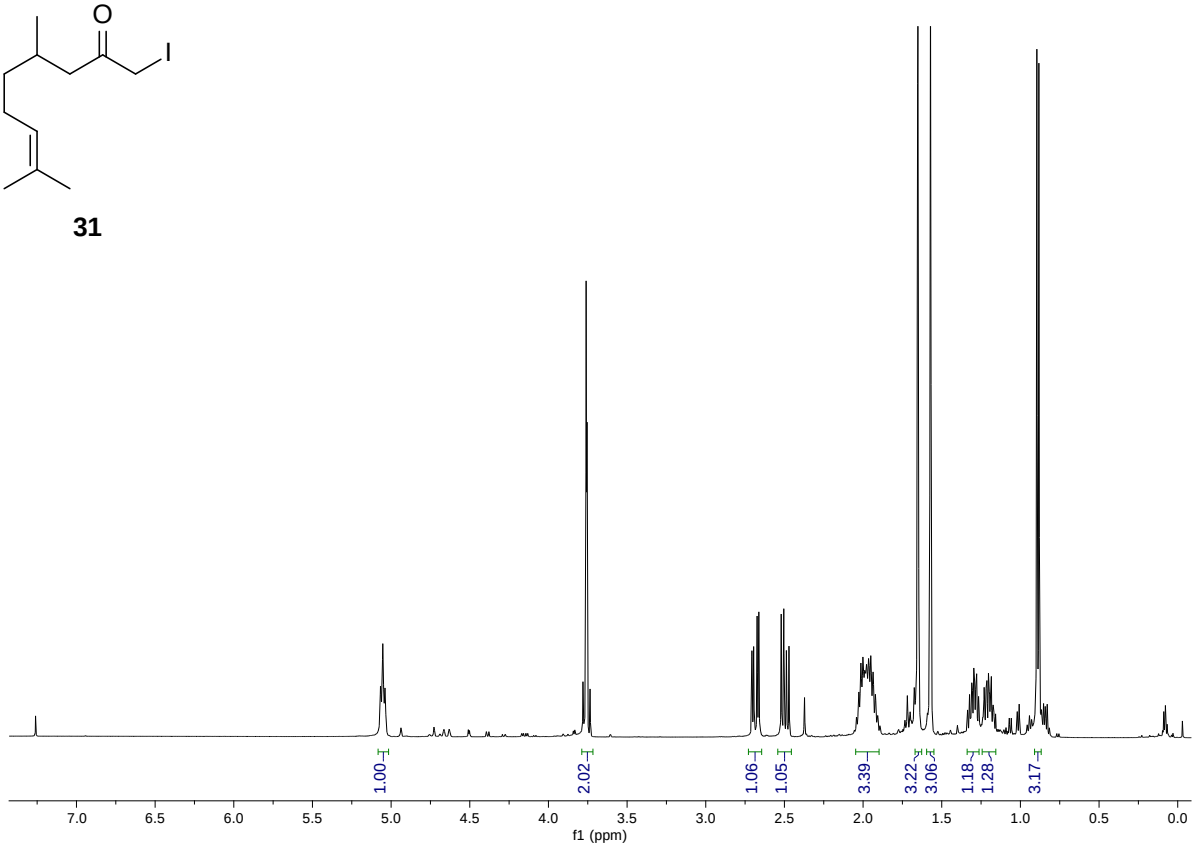

202.68
133.96
119.80
45.78
31.51
29.72
29.58
28.82
23.61
7.02
O
I
28
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
+
O
29
30
0.99
0.60
0.60
0.59
9.64
7.82
0.61
3.34
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


212.43
211.64
150.93
136.55
119.93
107.84
49.22
47.99
47.21
44.82
40.68
35.86
34.48
33.33
32.80
30.86
30.33
29.60
28.07
22.09
O
+
O
29
30
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

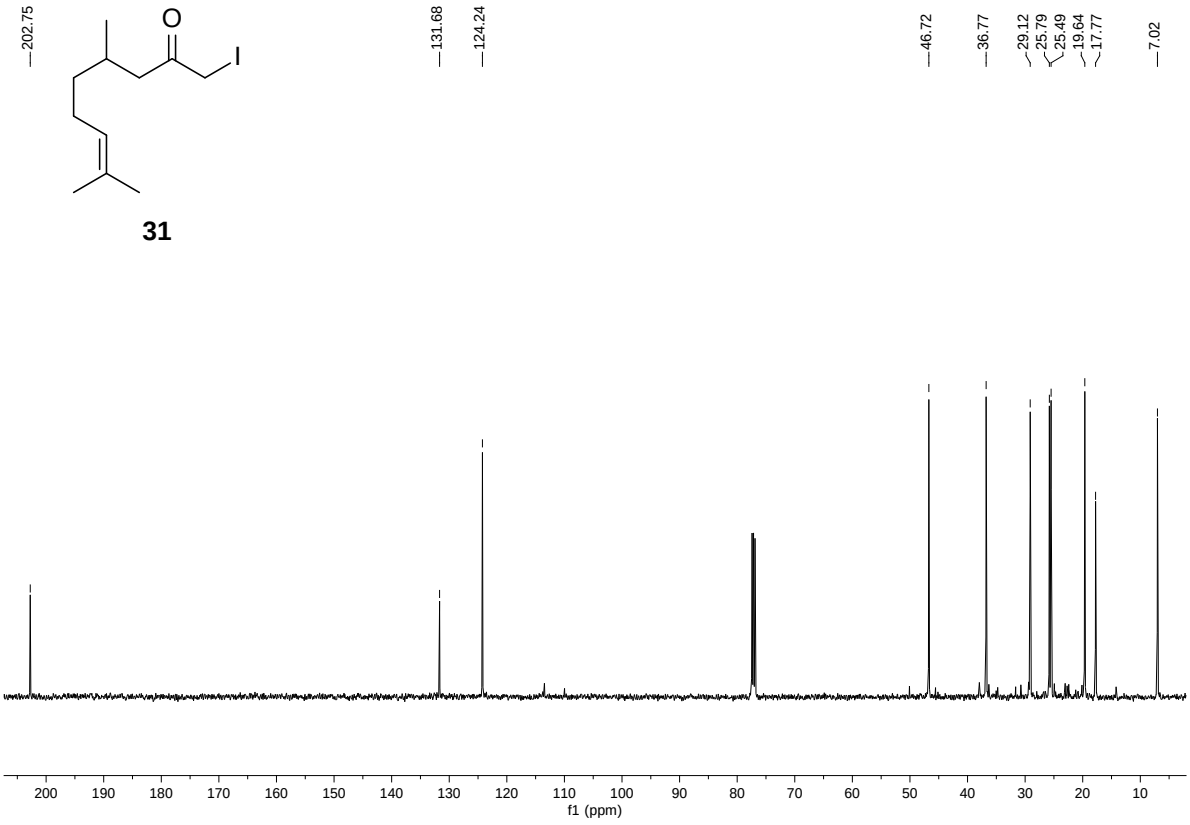

O
I

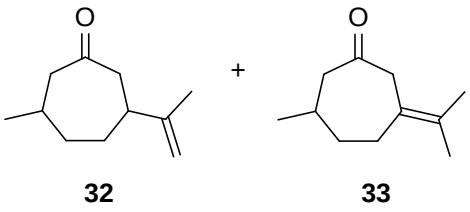
31


1.00
2.02
1.06
1.05
3.39
3.22
3.06
1.18
1.28
3.17
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

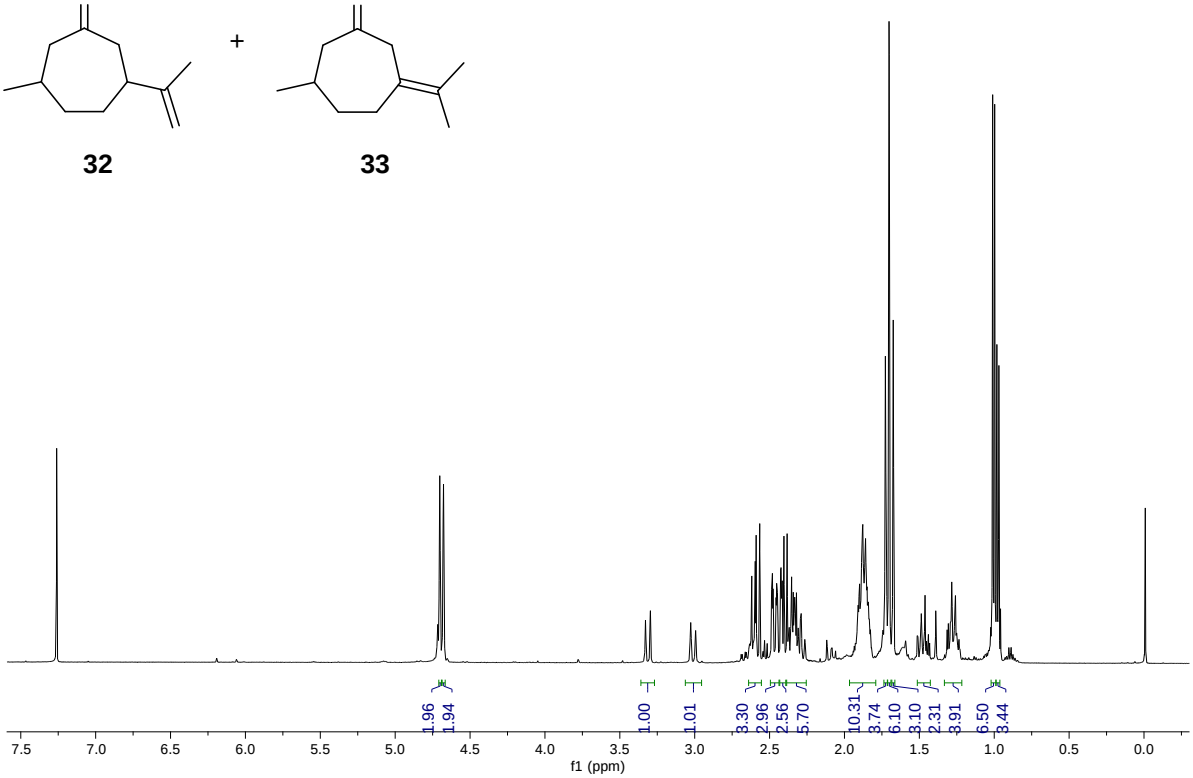
O
I

31

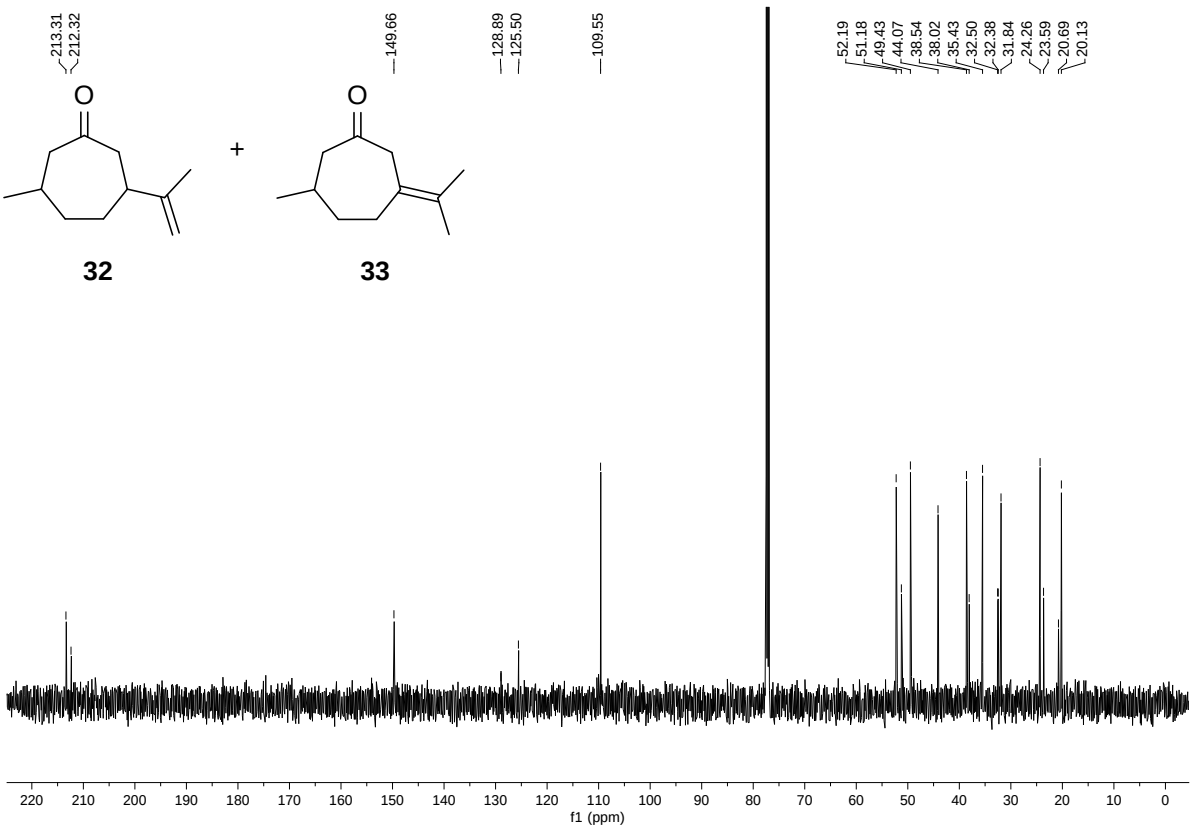

202.75
131.68
124.24
46.72
36.77
29.12
25.79
25.49
19.64
17.77
7.02
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

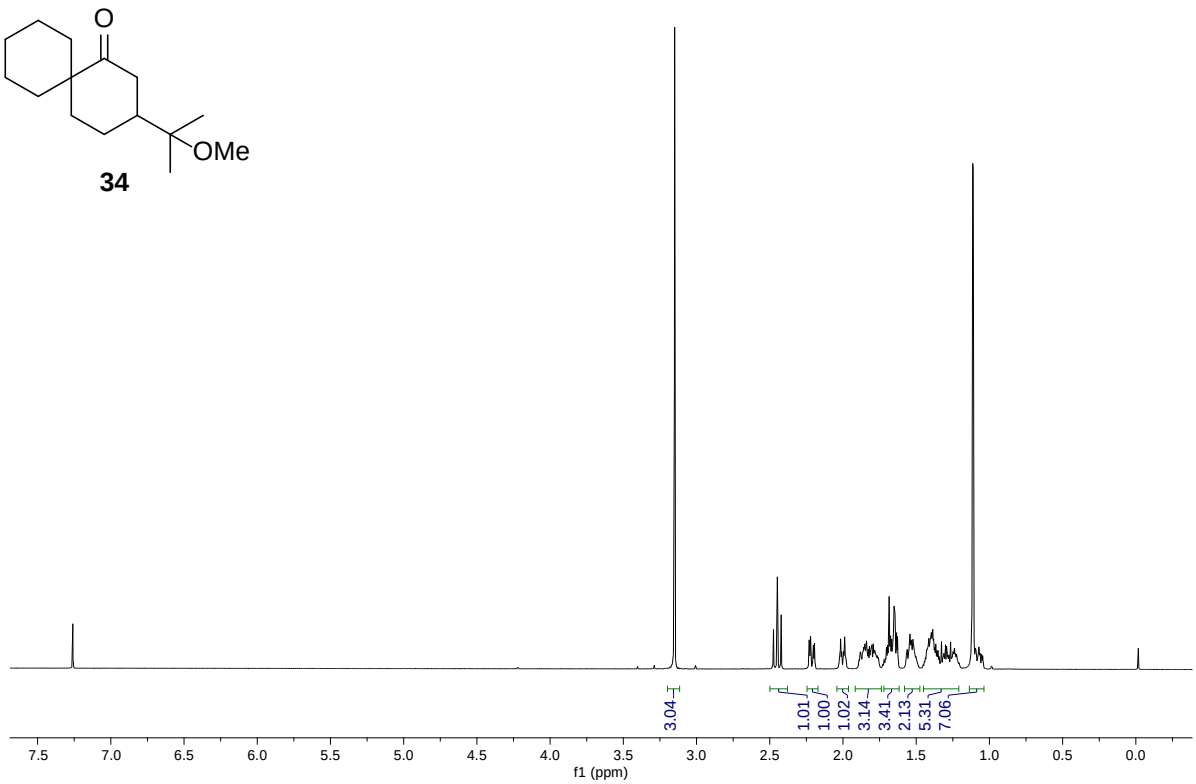


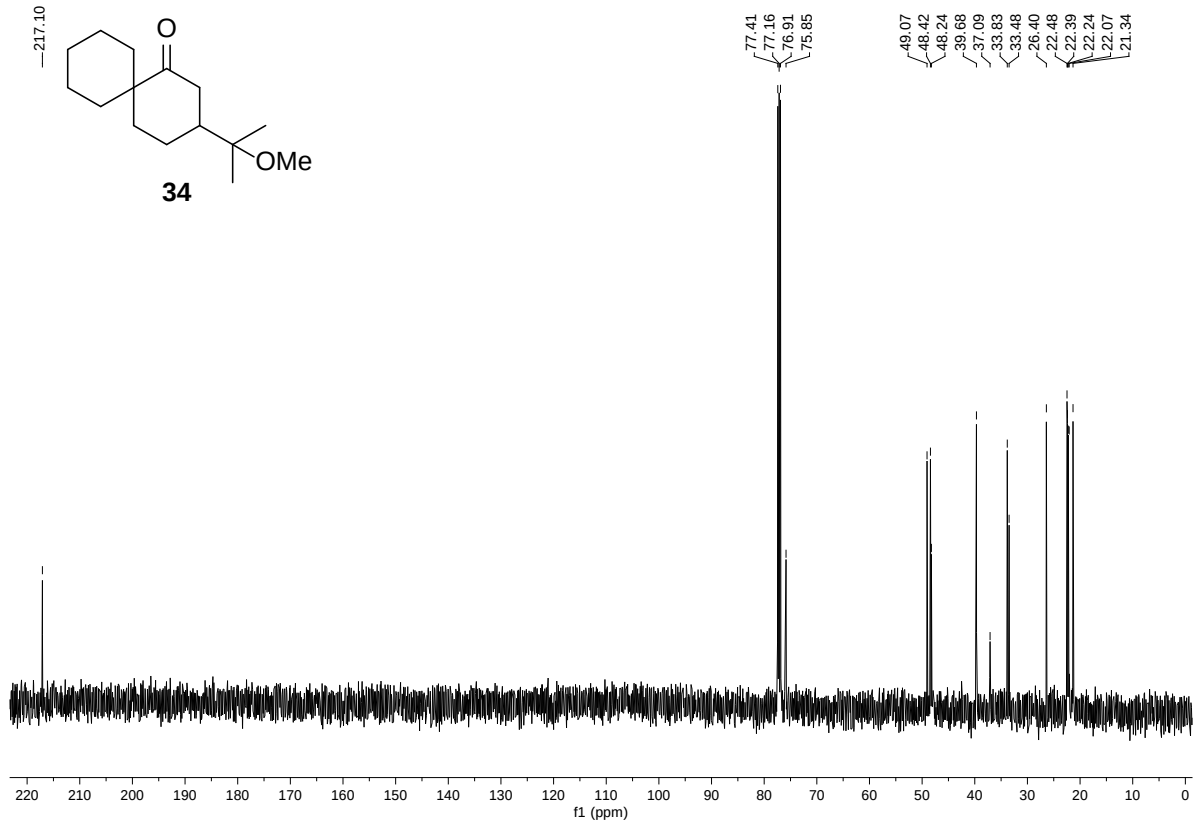
32 **33**

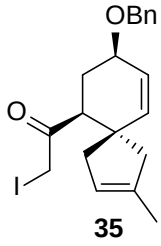

1.96
1.94
1.00
1.01
3.30
2.96
2.56
5.70
10.31
3.74
6.10
3.10
2.31
3.91
6.50
3.44
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

32 **33**

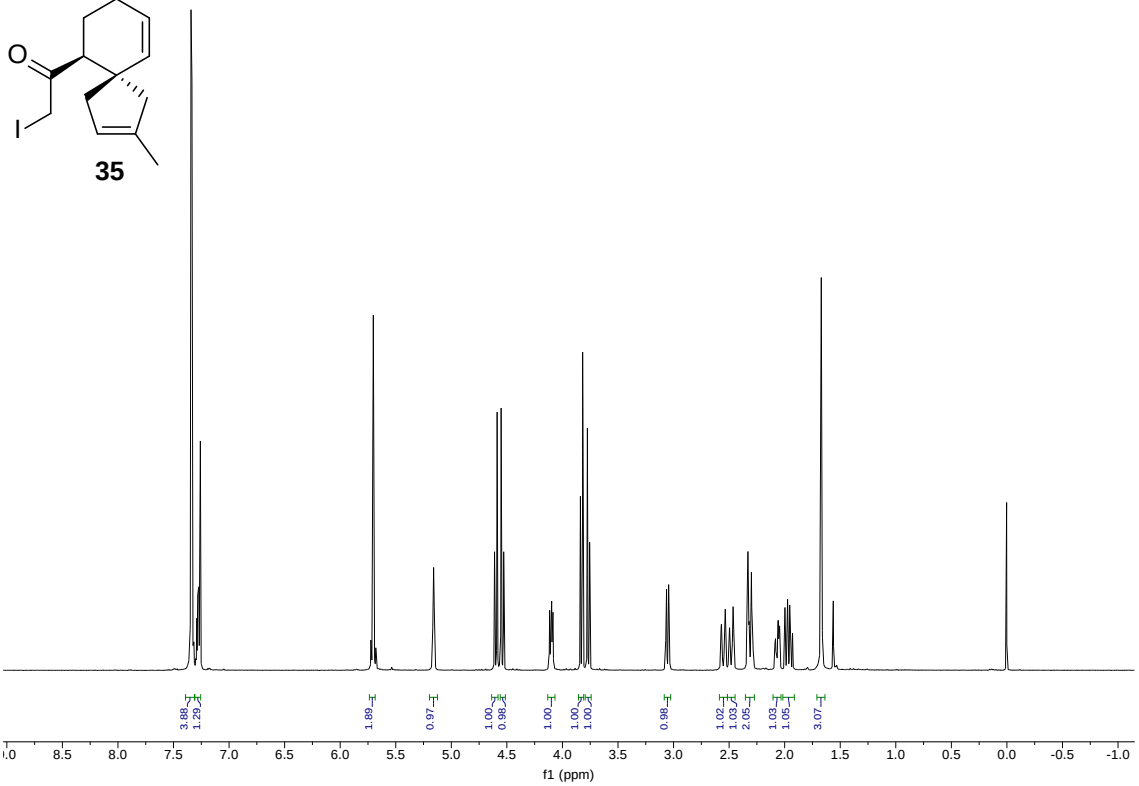

213.31
212.32
149.66
128.89
125.50
109.55
52.19
51.18
49.43
44.07
38.54
38.02
35.43
32.50
32.38
31.84
24.26
23.59
20.69
20.13
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

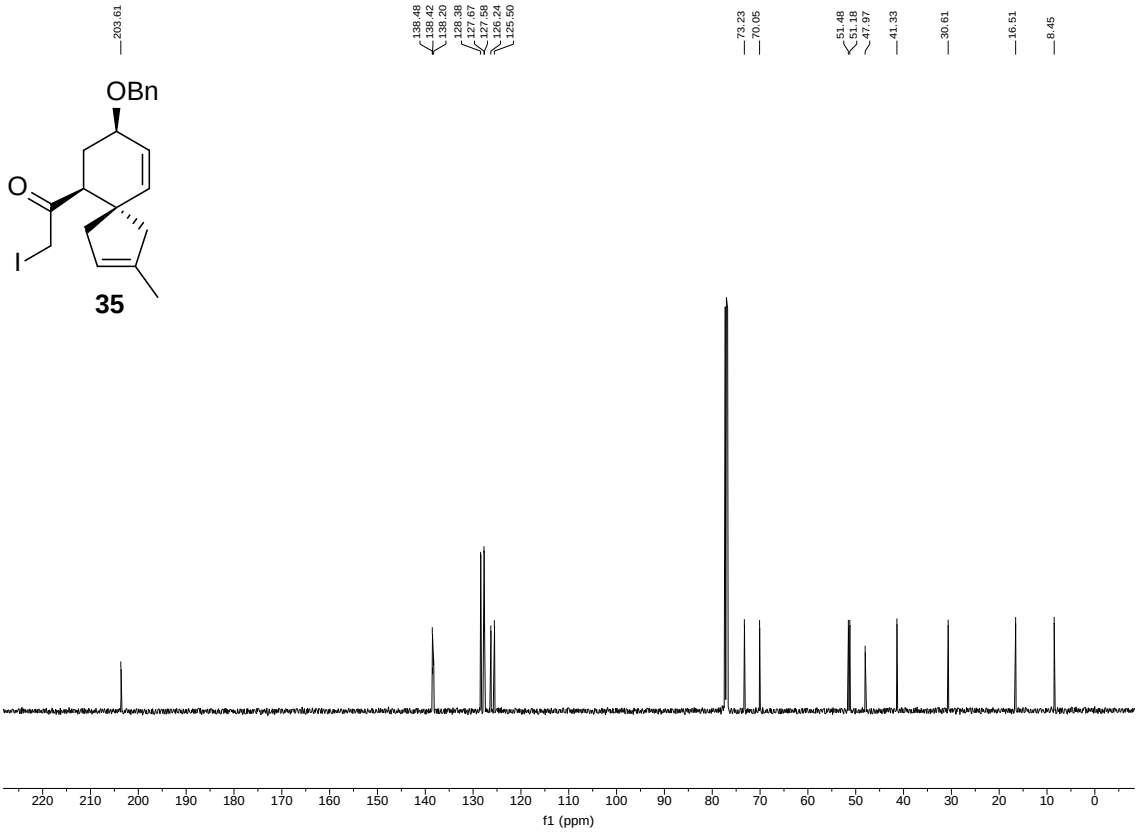

O
OMe
34
3.04
1.01
1.00
1.02
3.14
3.41
2.13
5.31
7.06
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


217.10
O
OMe
34
77.41
77.16
76.91
75.85
49.07
48.42
48.24
39.68
37.09
33.83
33.48
26.40
22.48
22.39
22.24
22.07
21.34
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OBn
O
I

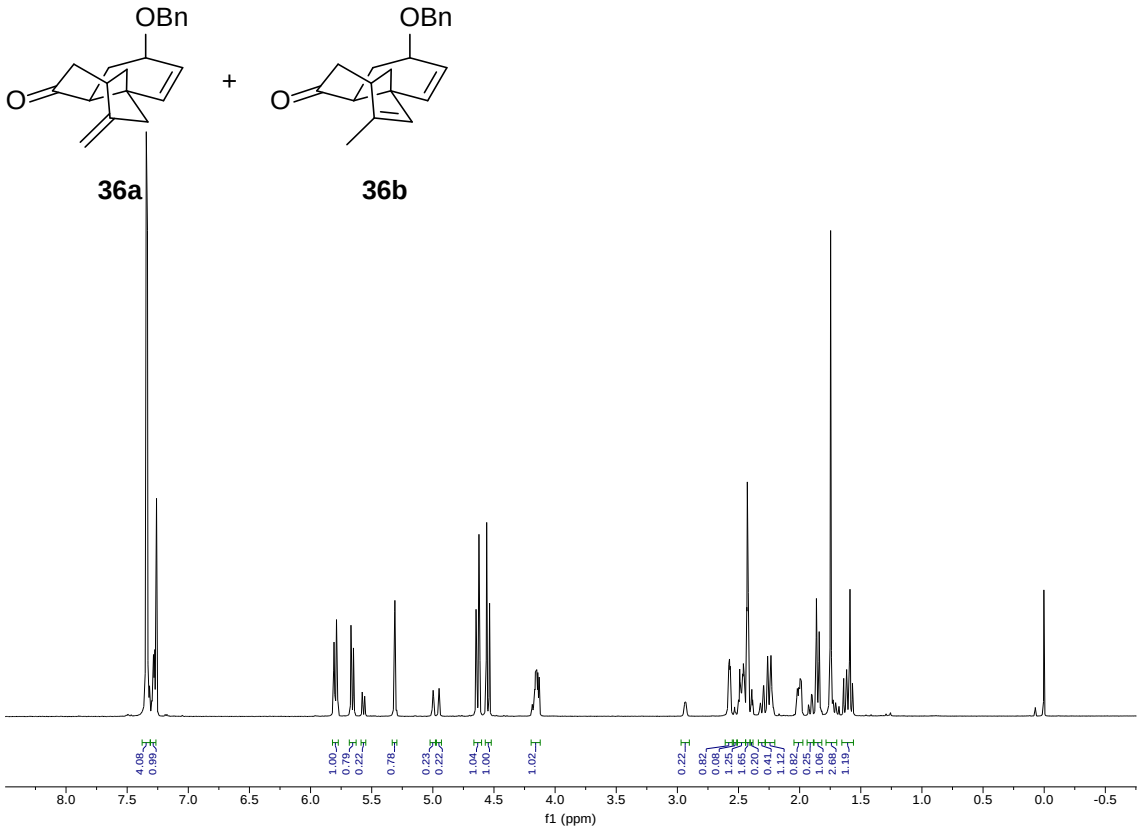
35

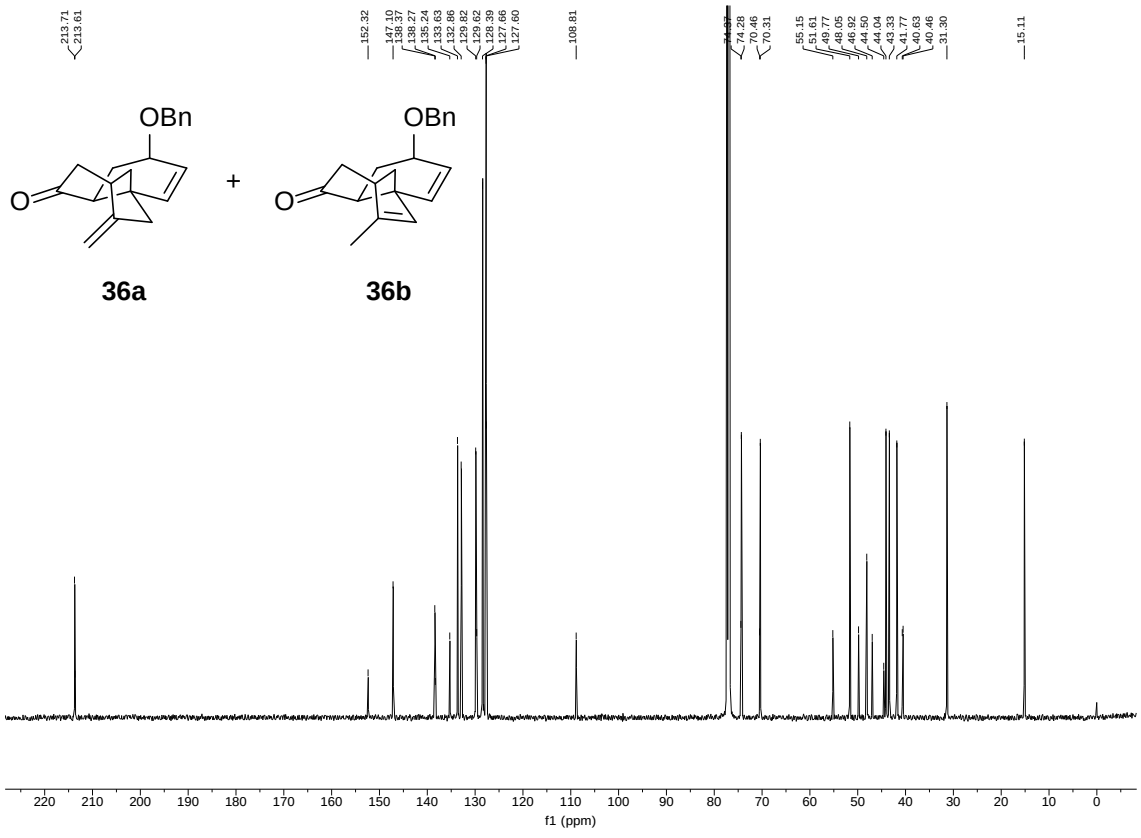

3.88
1.29
1.89
0.97
1.00
0.98
1.00
1.00
1.00
0.98
1.02
1.03
2.05
1.03
1.05
3.07
f1 (ppm)

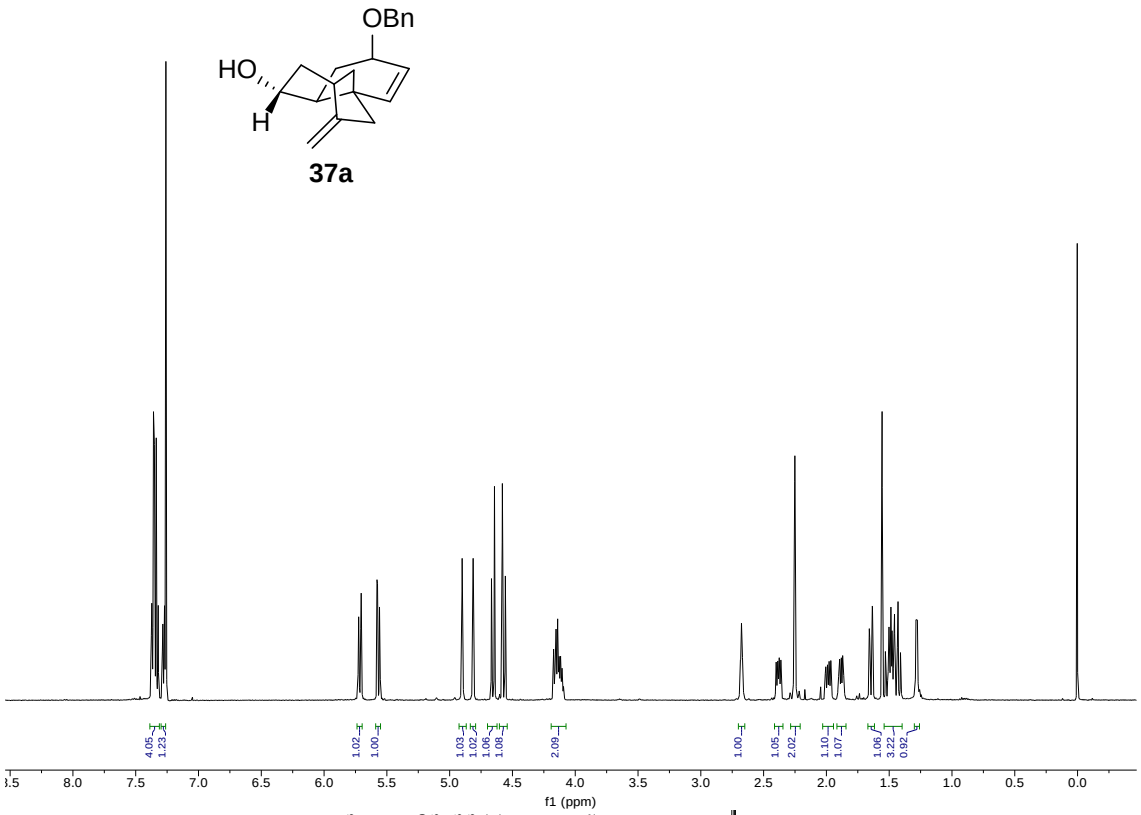

203.61
138.48
138.42
138.20
128.38
127.67
127.58
126.24
125.50
73.23
70.05
51.48
51.19
47.97
41.33
30.61
16.51
8.45
f1 (ppm)

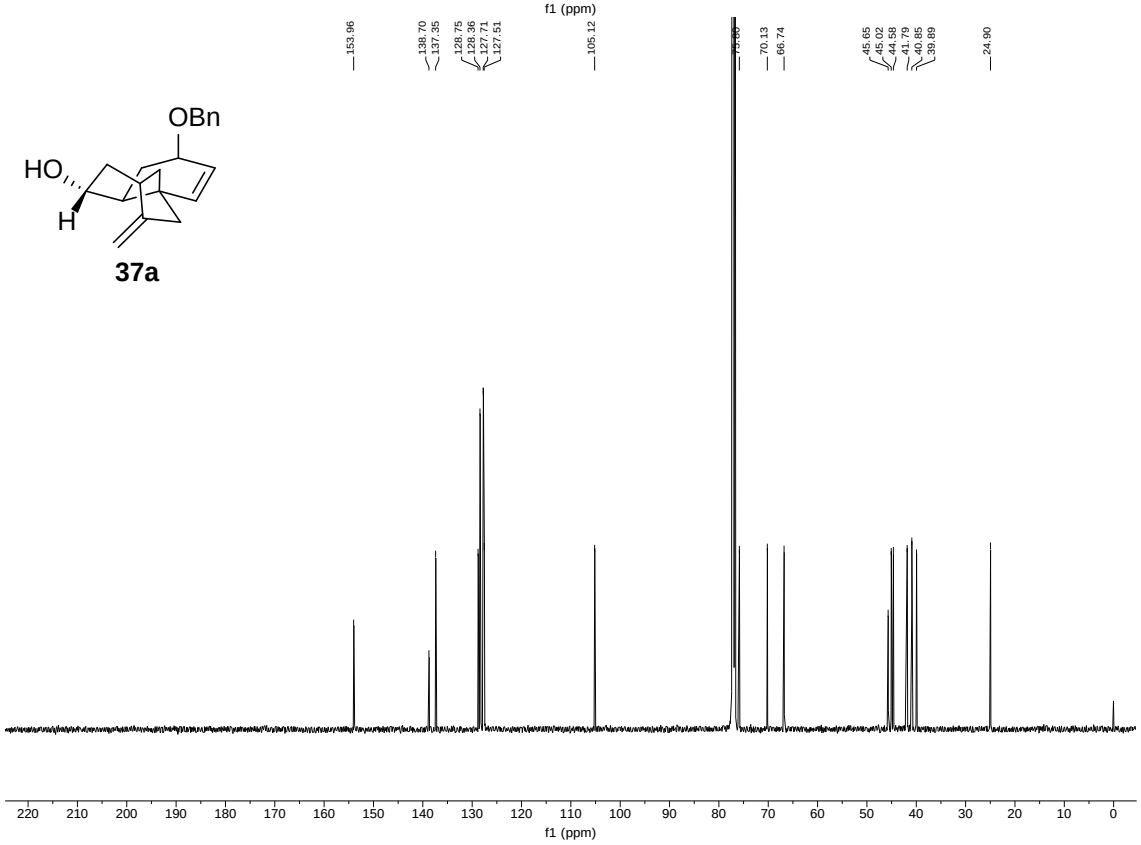
OBn
O
I

35

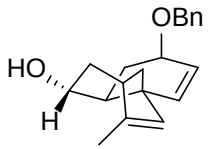

OBn
O
+
OBn
O
36a
36b
4.08
0.99
1.00
0.79
0.22
0.78
0.23
0.22
1.04
1.00
1.02
0.22
0.82
0.08
1.25
1.65
0.20
0.41
1.12
0.82
0.25
1.06
2.68
1.19
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


213.71
213.61
152.32
147.10
138.37
138.27
135.24
133.63
132.86
129.82
129.62
128.39
127.66
127.60
108.81
74.97
74.28
70.46
70.31
55.15
51.61
49.77
48.05
46.92
44.50
44.04
43.33
41.77
40.63
40.46
31.30
15.11
OBn
O
+
OBn
O
36a
36b
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

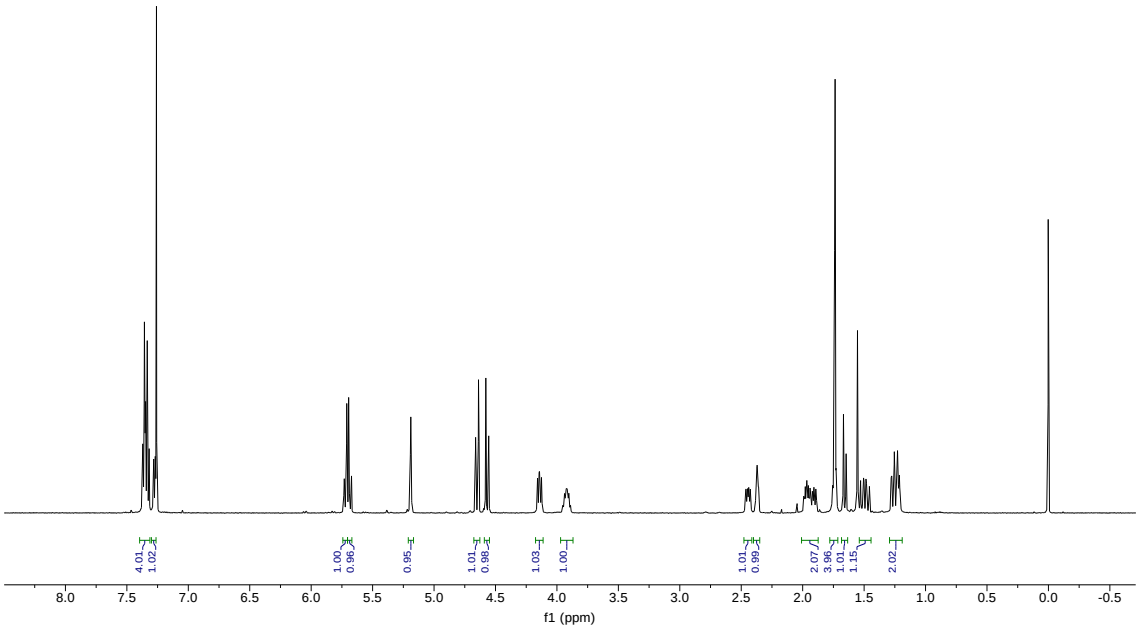

OBn
HO
H
37a
4.05
1.23
1.02
1.00
1.03
1.02
1.06
1.08
2.09
1.00
1.05
2.02
1.10
1.07
1.06
3.22
0.92
f1 (ppm)

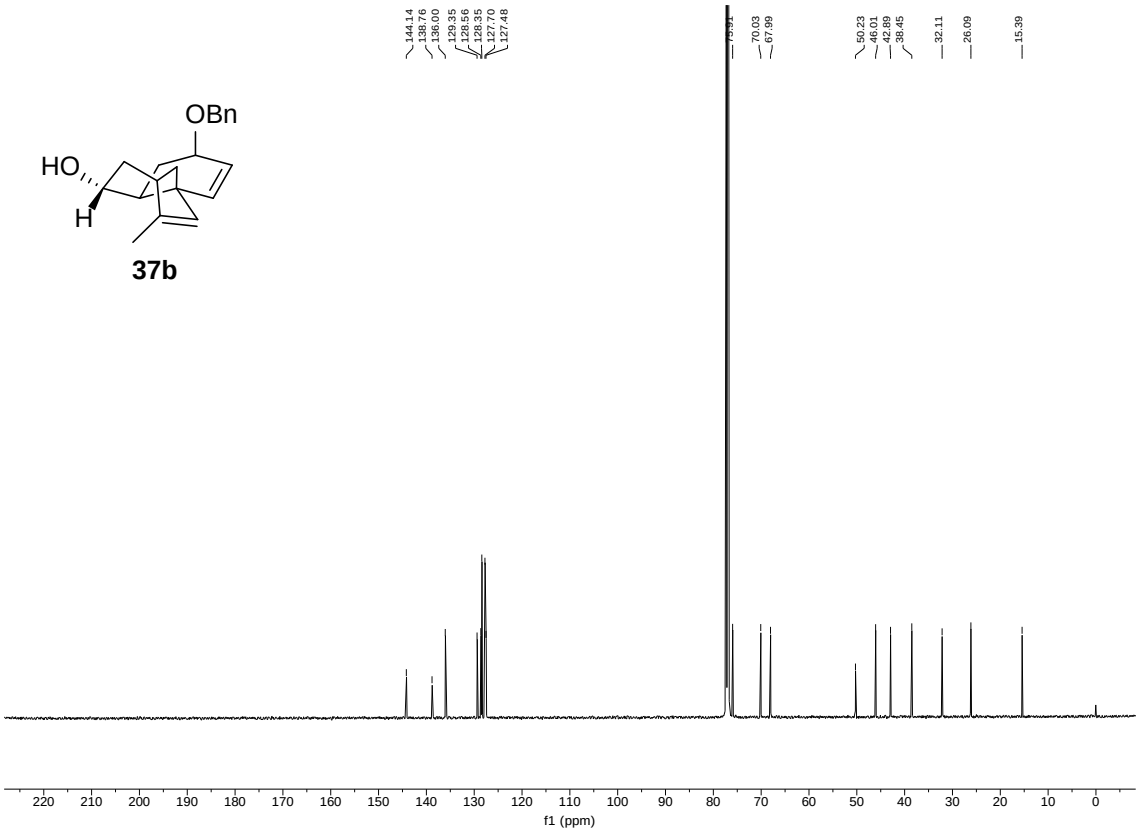

153.96
138.70
137.35
128.75
128.36
127.71
127.51
105.12
70.13
66.74
45.65
45.02
44.58
41.79
40.85
39.89
24.90
f1 (ppm)

OBn
HO
H
37a


OBn
HO
H

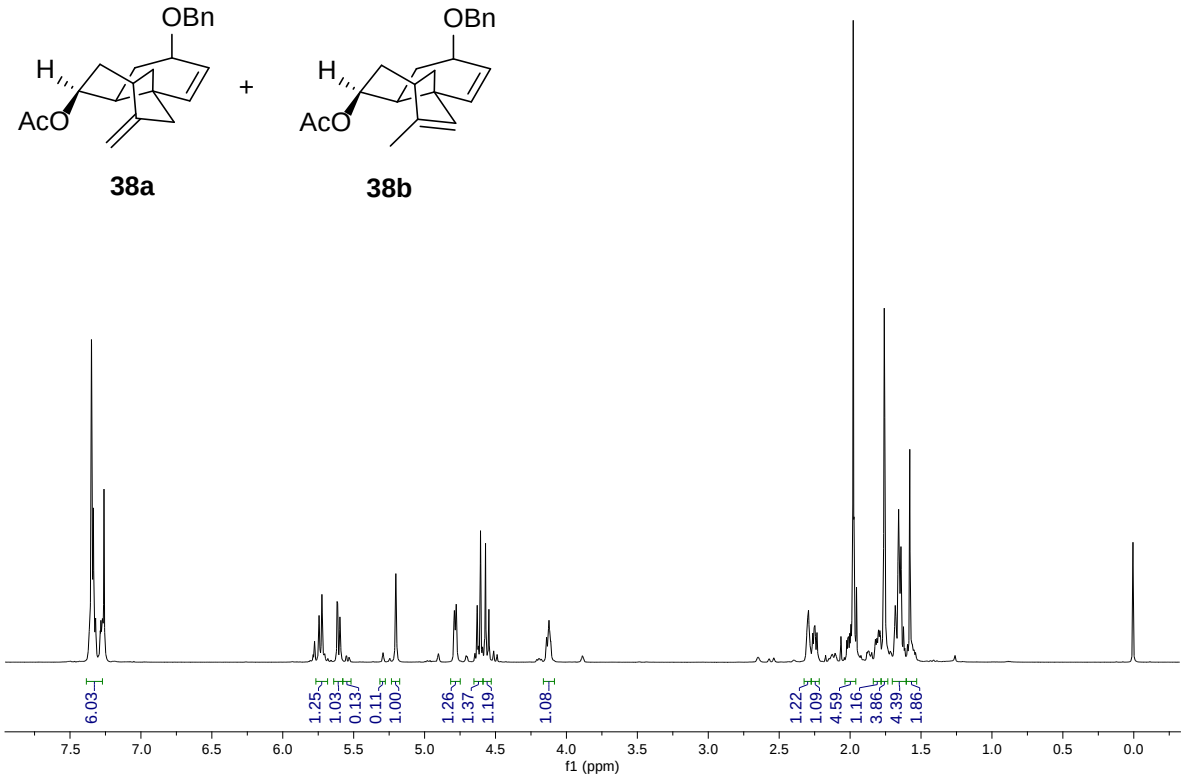
37b

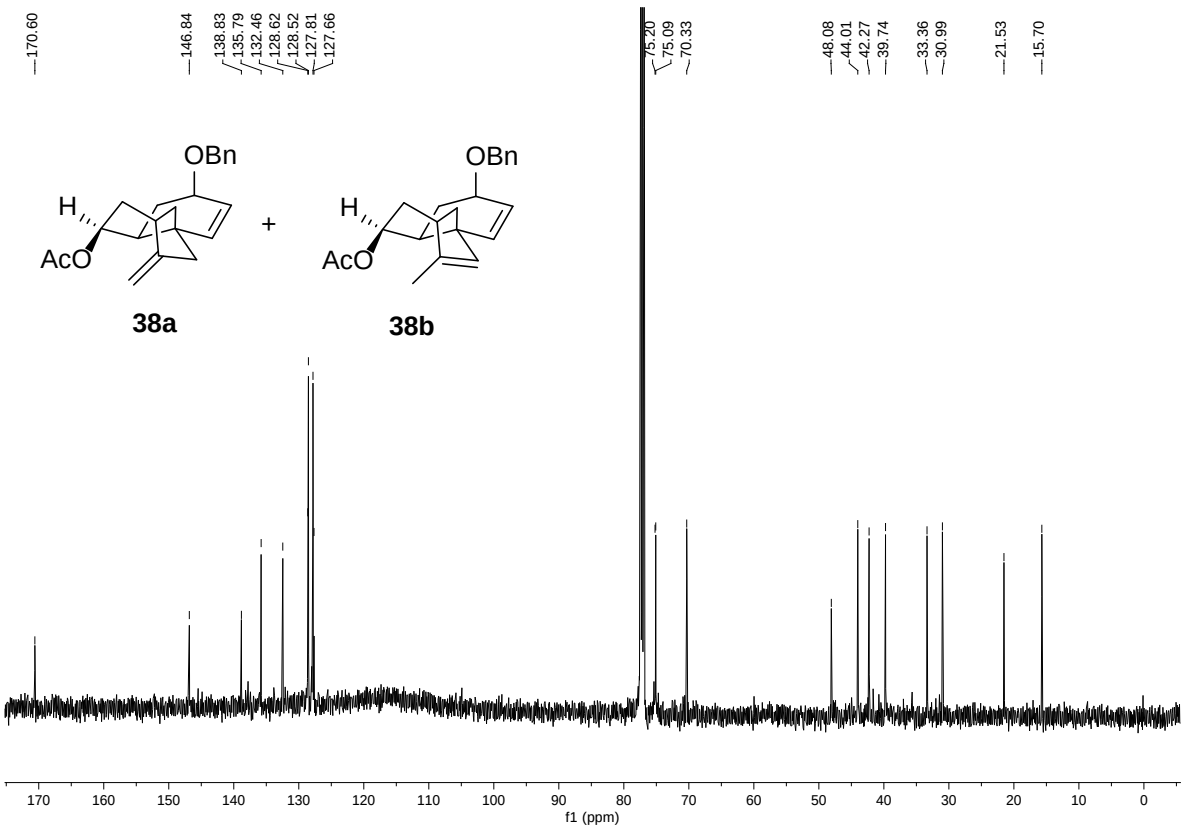

4.01
1.02
1.00
0.90
0.95
1.01
0.98
1.03
1.00
1.01
0.99
2.07
3.96
1.01
1.15
2.02
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

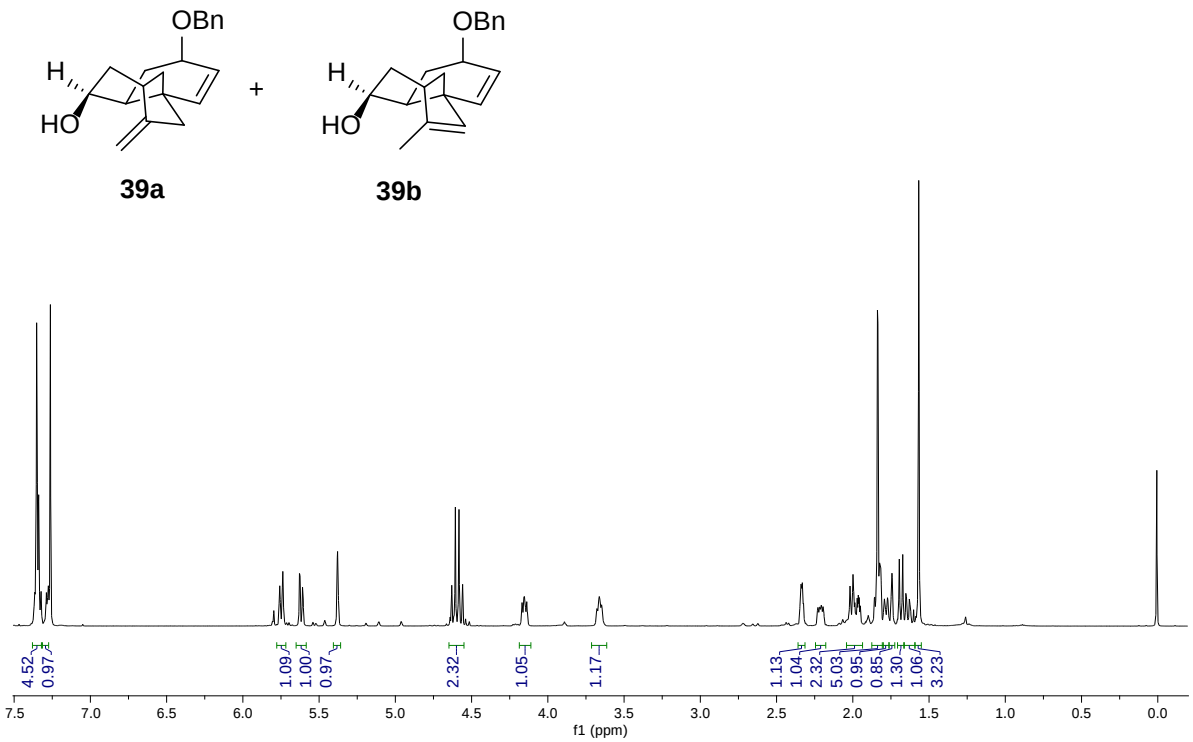

144.14
138.76
138.00
129.35
128.56
128.35
127.70
127.48
79.91
70.03
67.99
50.23
46.01
42.89
38.45
32.11
26.09
15.39
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

OBn
HO
H

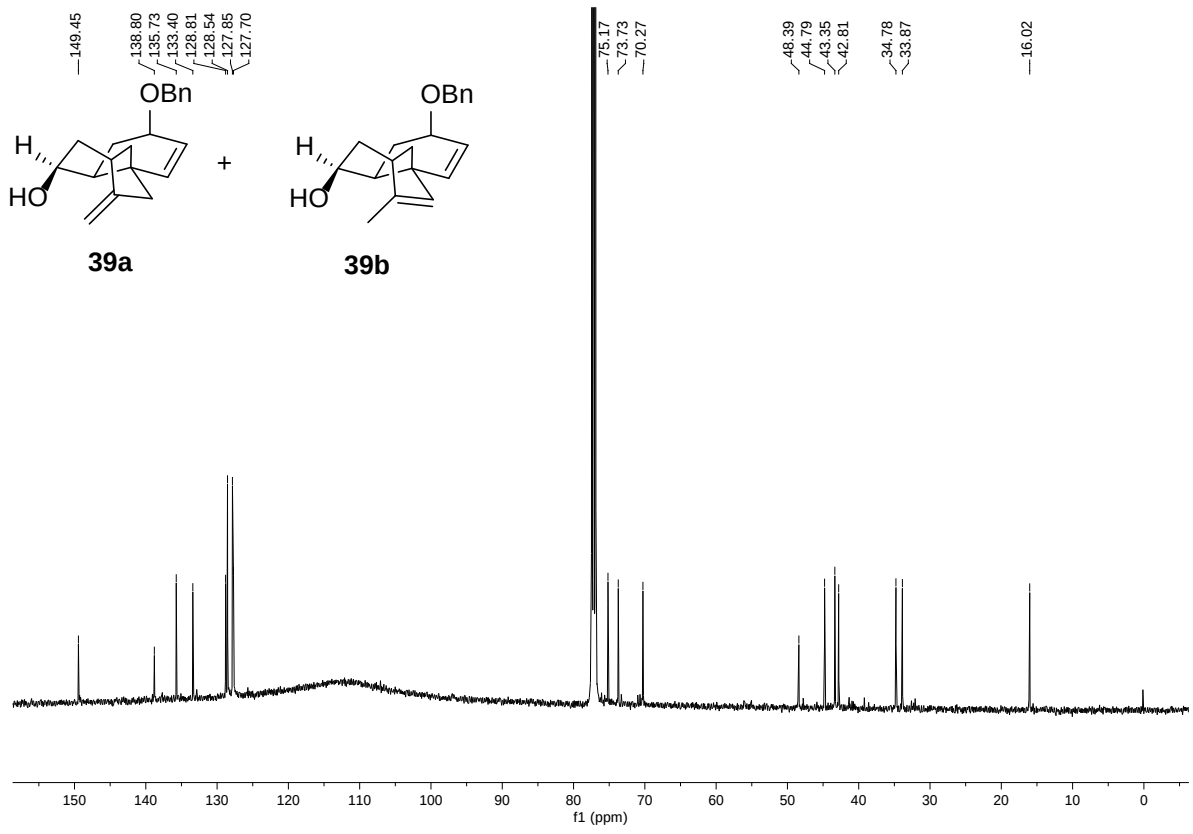
37b


OBn
H
AcO
+
OBn
H
AcO
38a
38b
6.03
1.25
1.03
0.13
0.11
1.00
1.26
1.37
1.19
1.08
1.22
1.09
4.59
1.16
3.86
4.39
1.86
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


170.60
146.84
138.83
135.79
132.46
128.62
128.52
127.81
127.66
75.20
75.09
70.33
48.08
44.01
42.27
39.74
33.36
30.99
21.53
15.70
OBn
H
AcO
+
OBn
H
AcO
38a
38b
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



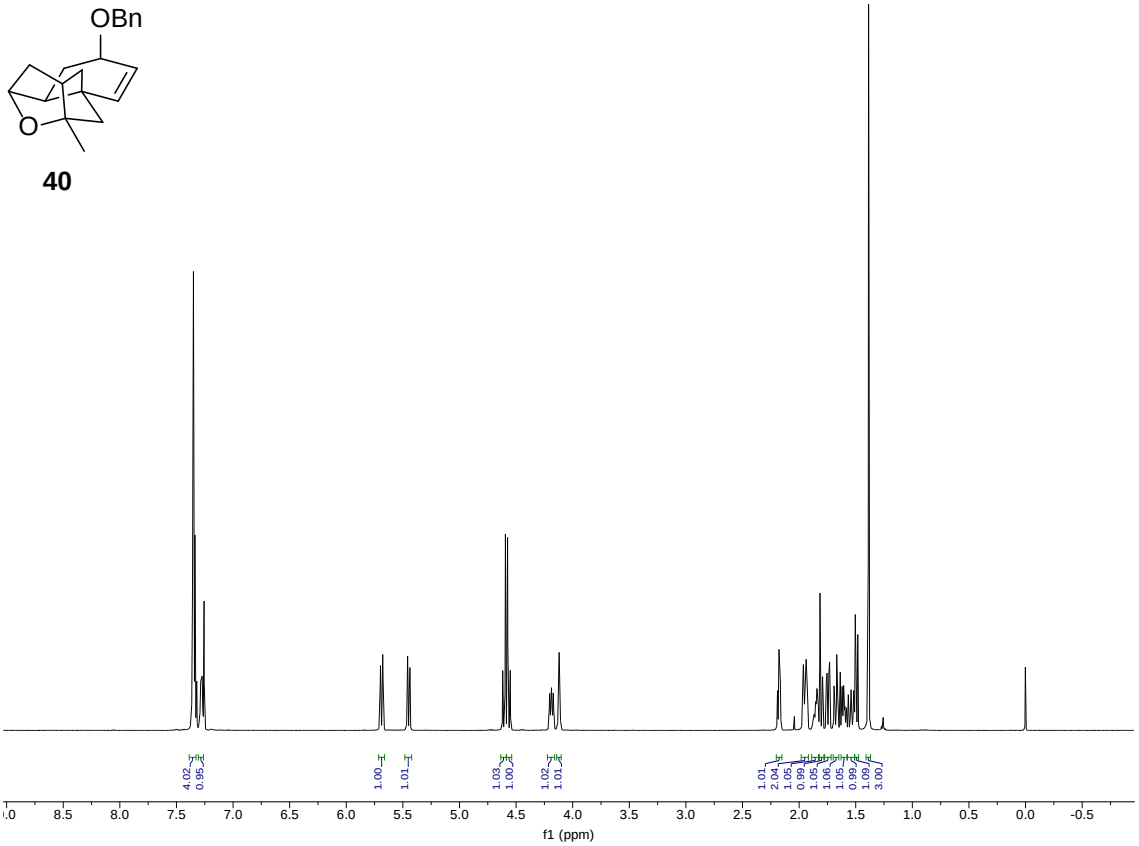
39a **39b**

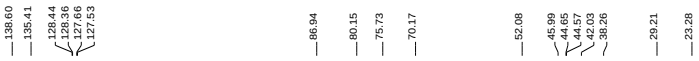


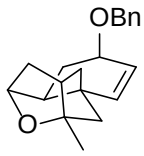
39a **39b**

OBn
O

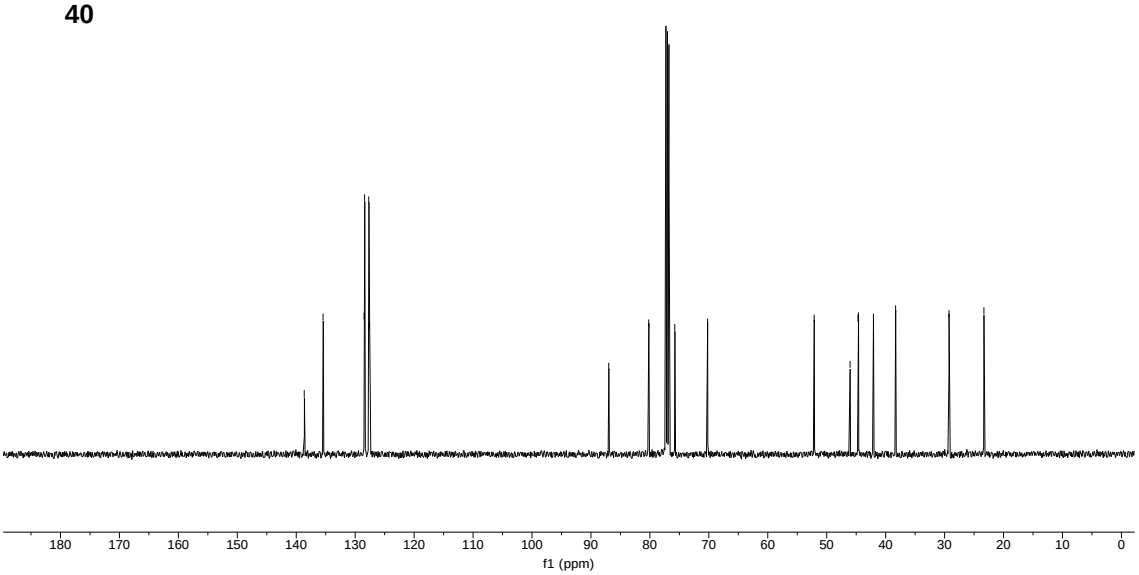
40


4.02
0.95
1.00
1.01
1.03
1.00
1.02
1.01
1.01
2.04
1.05
0.99
1.06
1.06
0.99
1.09
3.00
f1 (ppm)


138.60
135.41
128.44
128.36
127.66
127.53
86.94
80.15
75.73
70.17
52.08
45.99
44.65
44.57
42.03
38.26
29.21
23.28

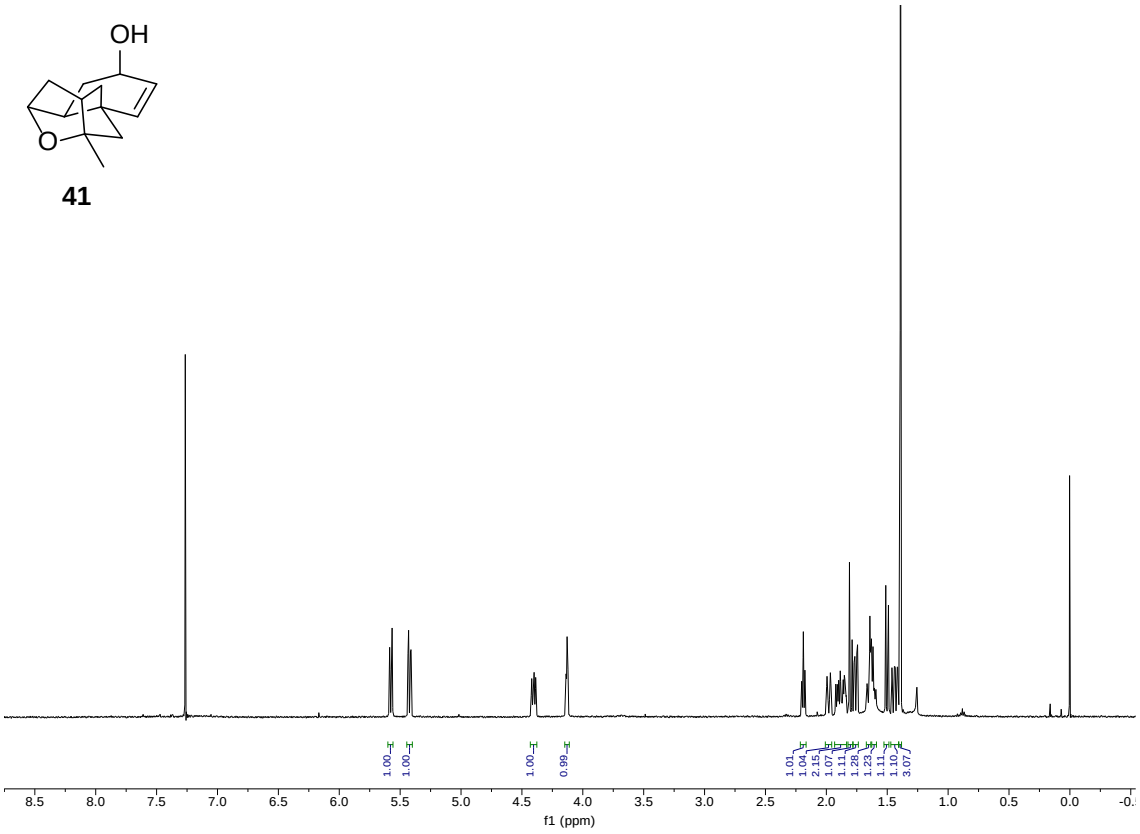

OBn
O

40


f1 (ppm)

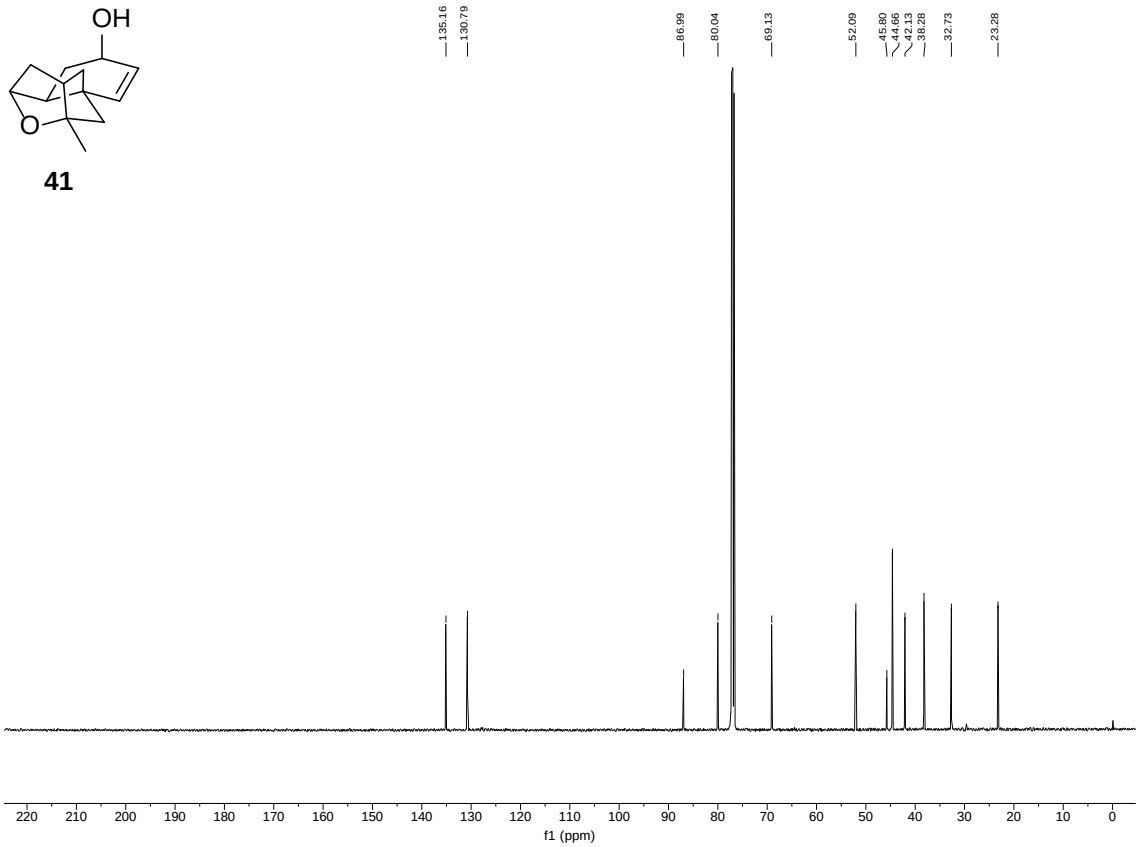
OH
O

41


1.00
1.00
1.00
0.99
1.01
1.04
2.15
1.07
1.11
1.29
1.23
1.11
1.10
3.07
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

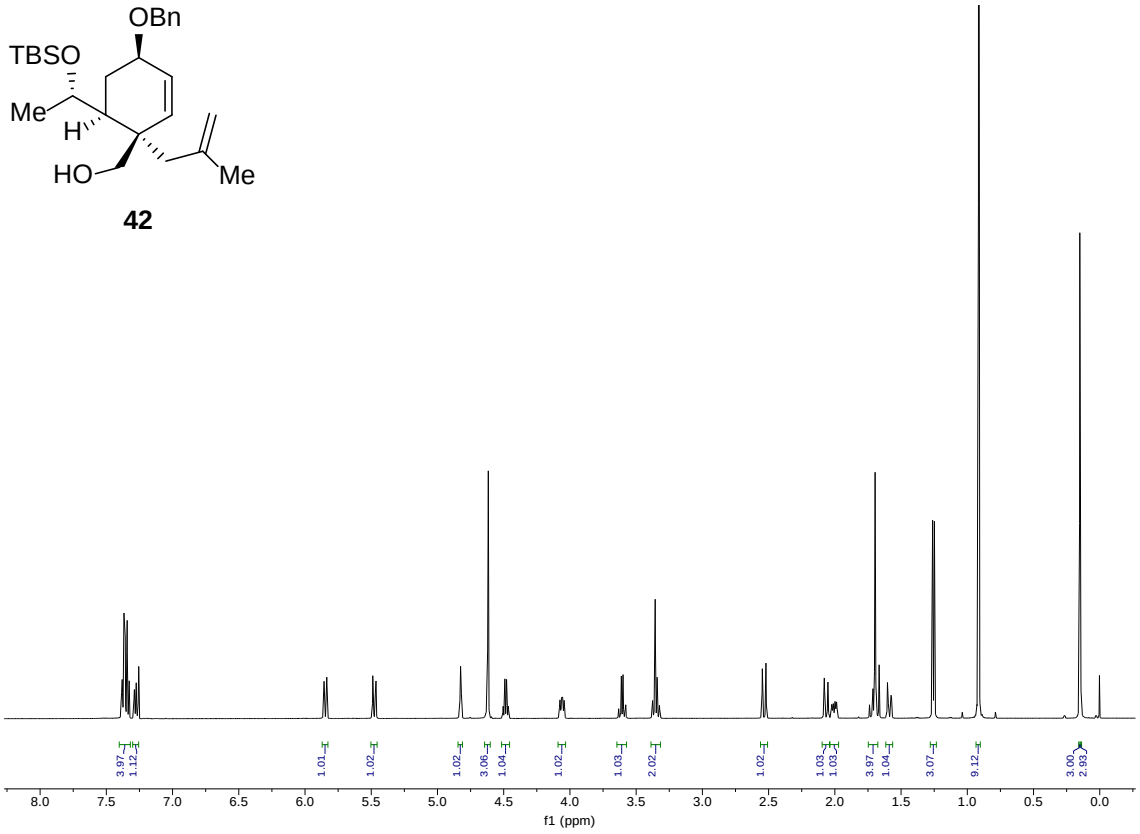
OH
O

41


135.16
130.79
86.99
80.04
69.13
52.09
45.90
44.66
42.13
38.28
32.73
23.28
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

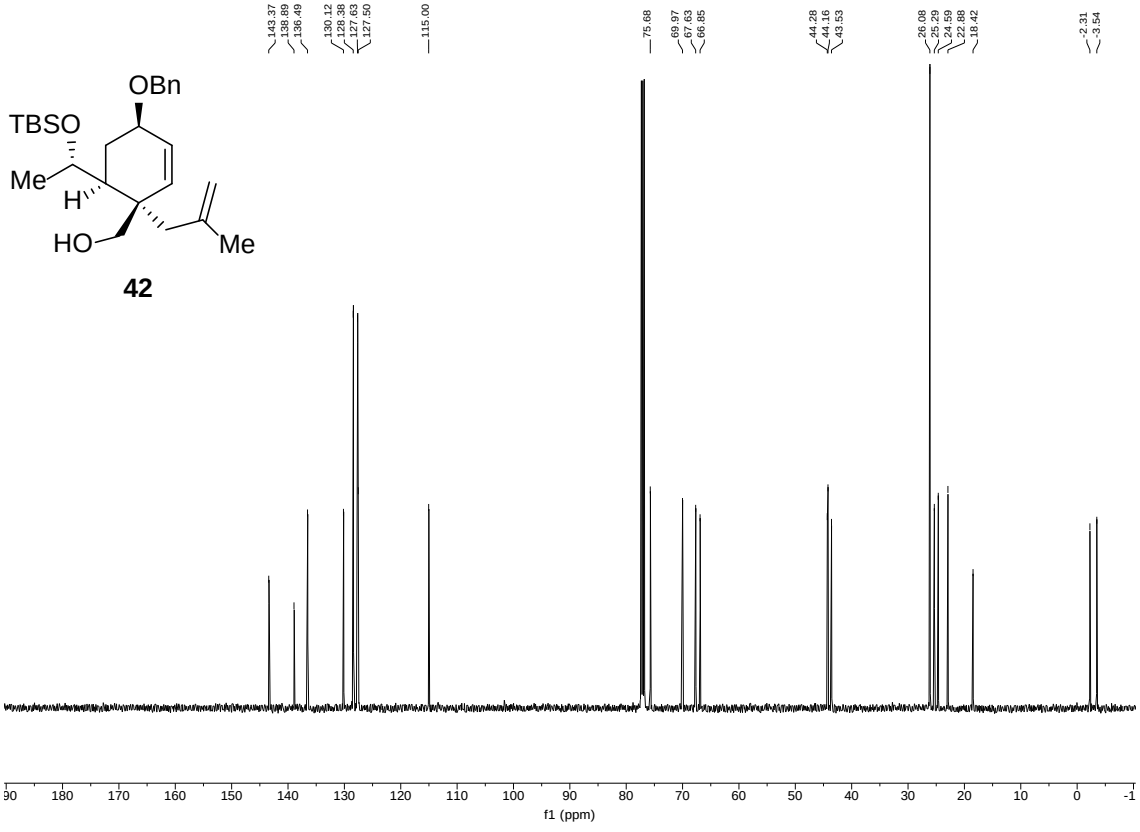
OBn
TBSO
Me
H
HO
Me

42

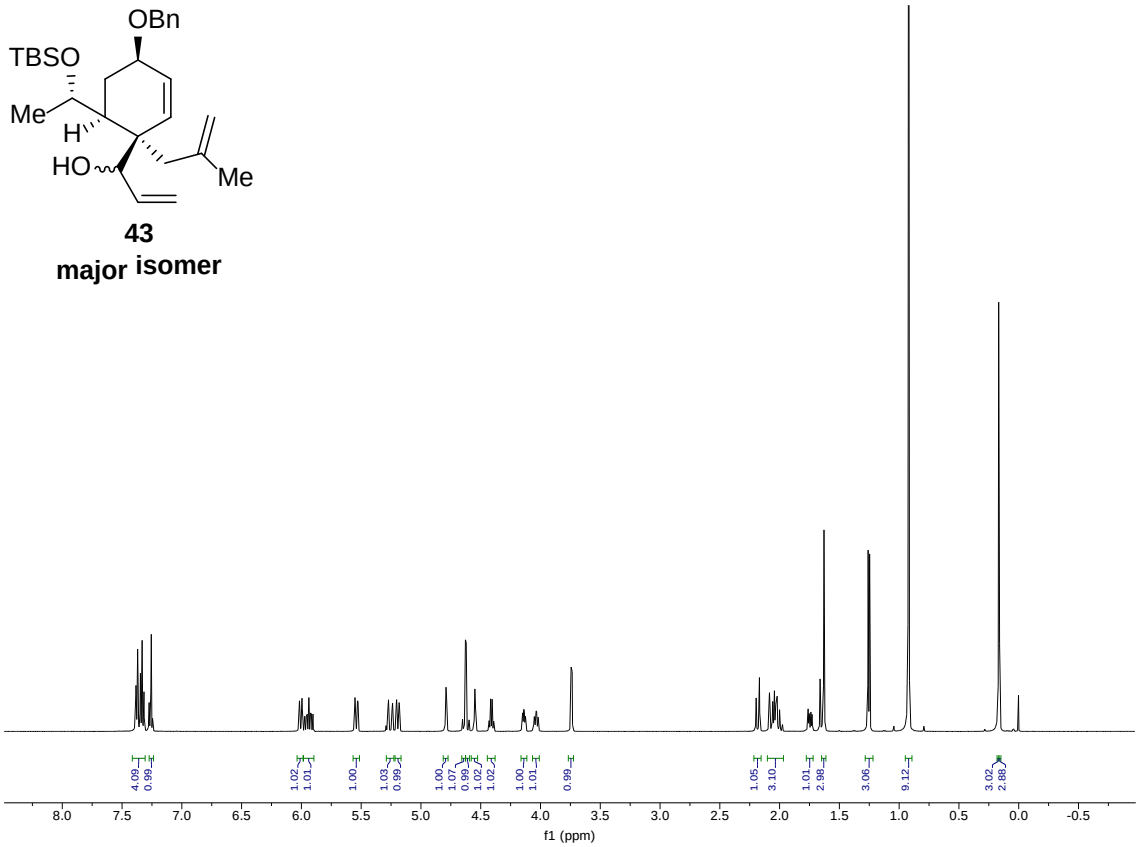

3.97
1.12
1.01
1.02
1.02
3.06
1.04
1.02
1.03
2.02
1.02
1.03
1.03
3.97
1.04
3.07
9.12
3.00
2.93
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

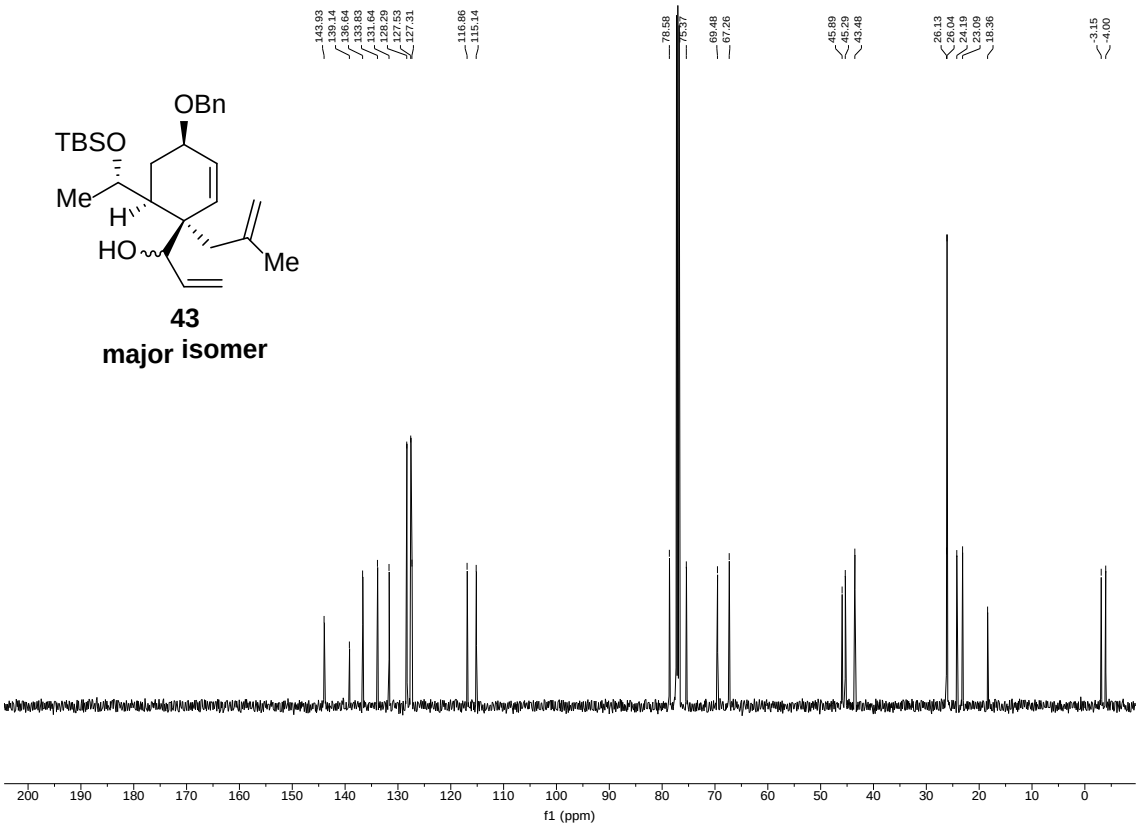
OBn
TBSO
Me
H
HO
Me

42


143.37
138.89
136.49
130.12
128.38
127.63
127.50
115.00
75.68
69.97
67.63
66.85
44.28
44.16
43.53
26.08
25.29
24.59
22.88
18.42
2.31
3.54
f1 (ppm)

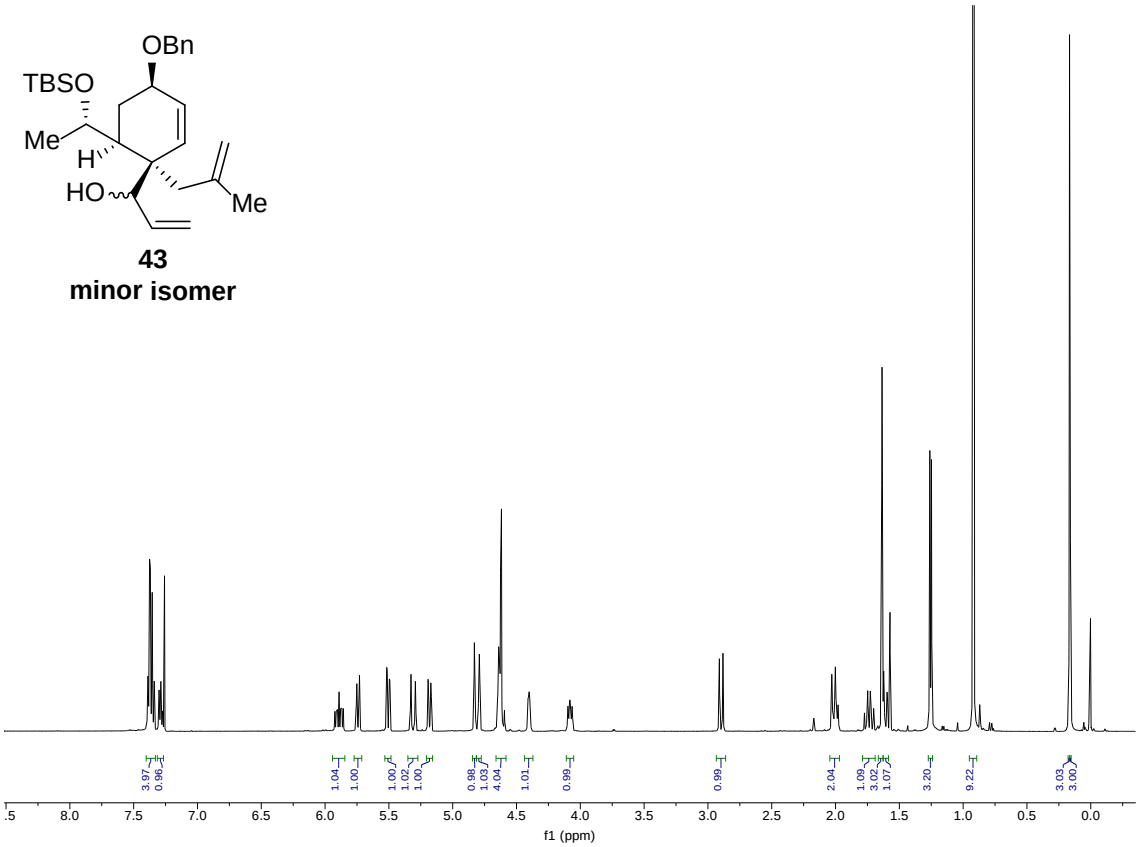
43
major isomer

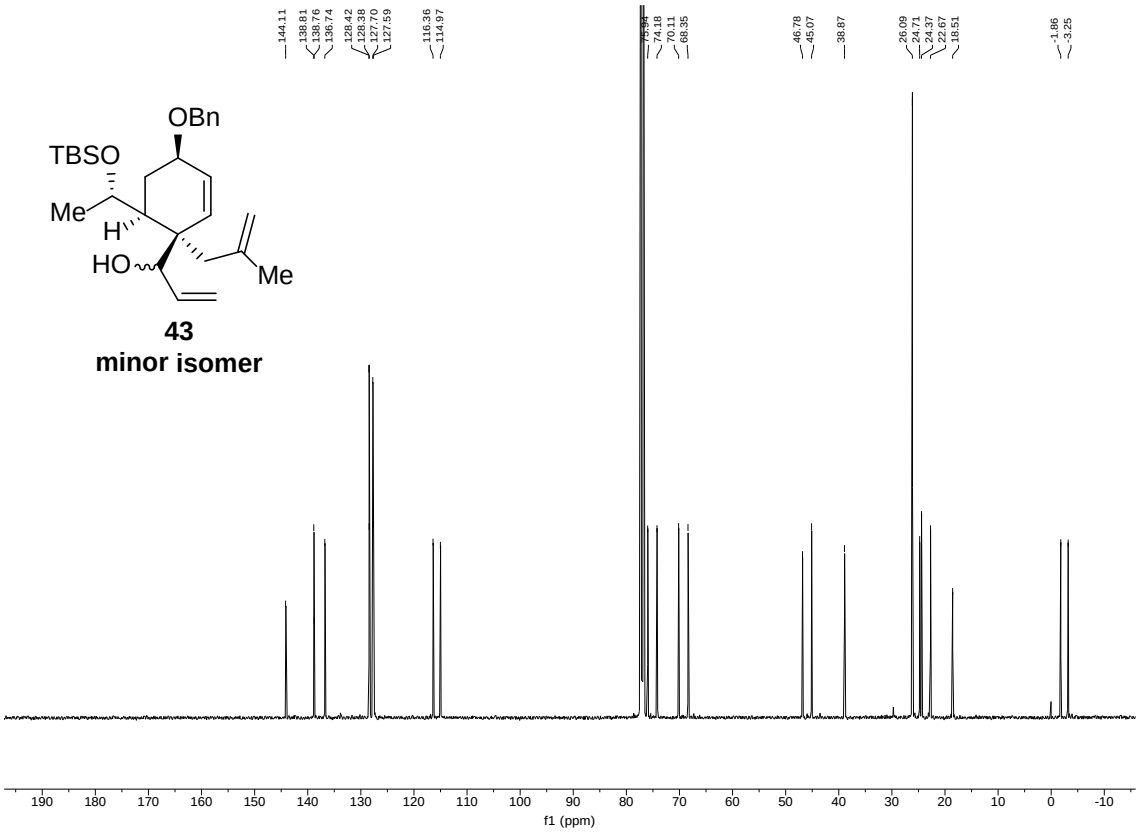




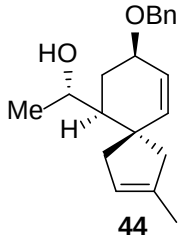
43
major isomer

43
minor isomer

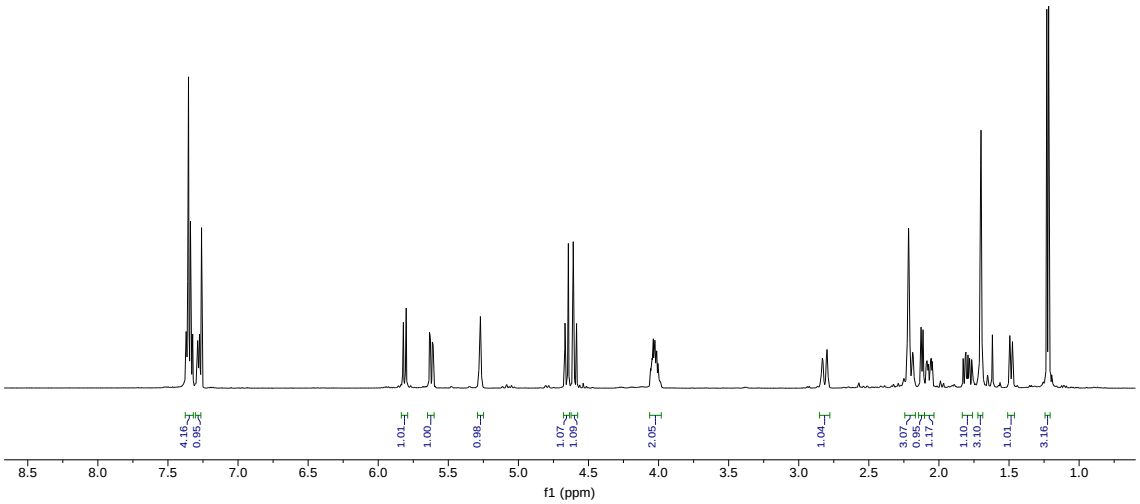




43
minor isomer

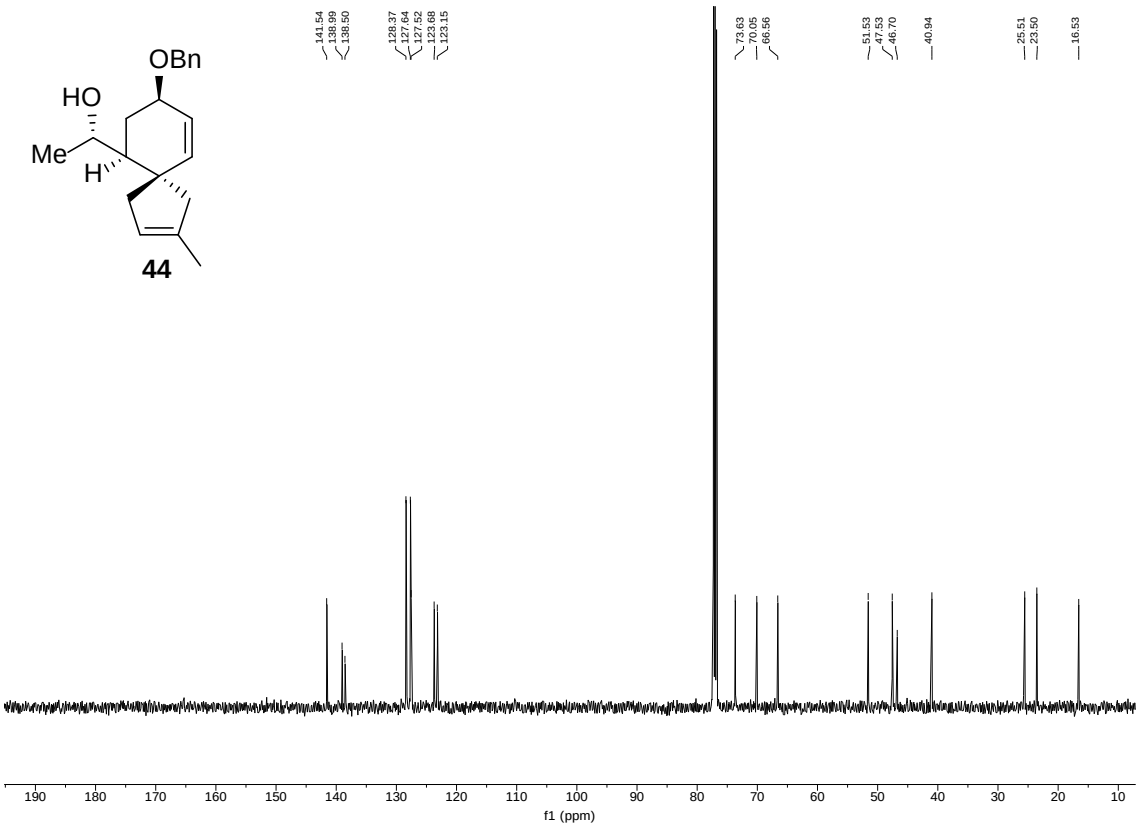

OBn
HO
Me
H

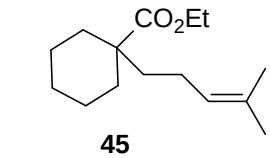
44


4.16
0.99
1.01
1.00
0.98
1.07
1.09
2.05
1.04
3.07
0.95
1.17
1.10
3.10
1.01
3.16
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

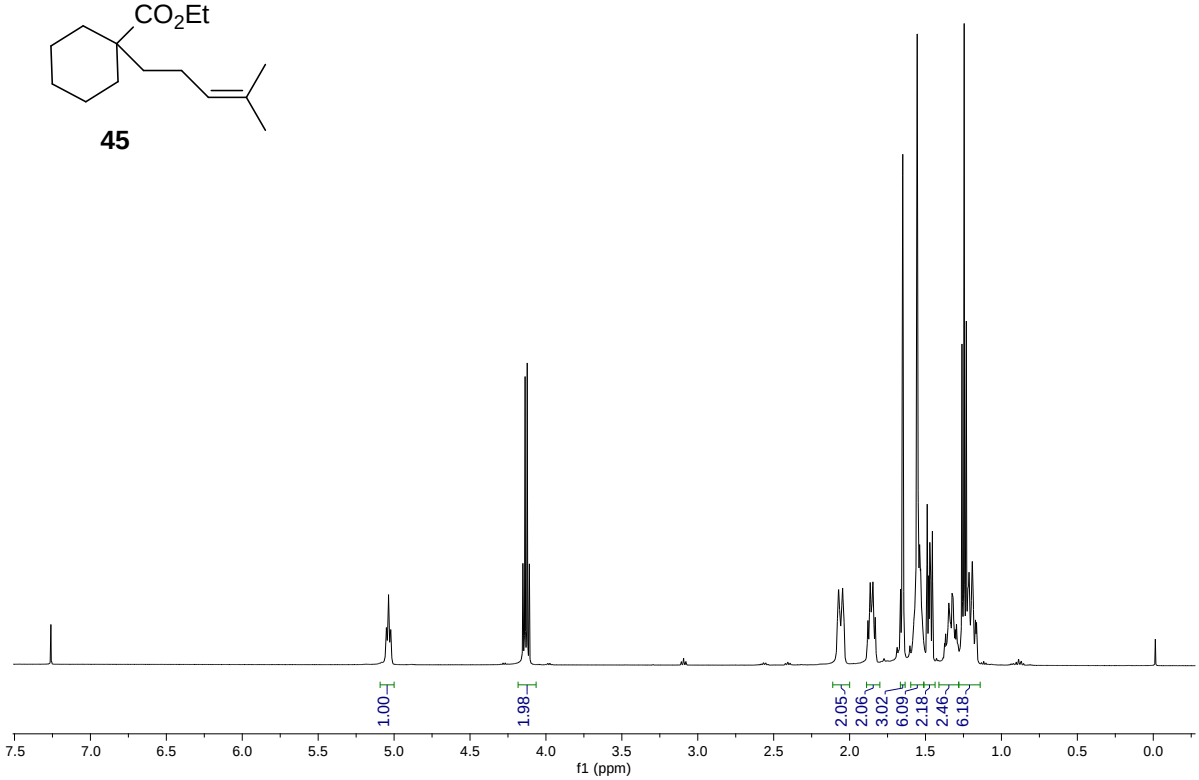
OBn
HO
Me
H

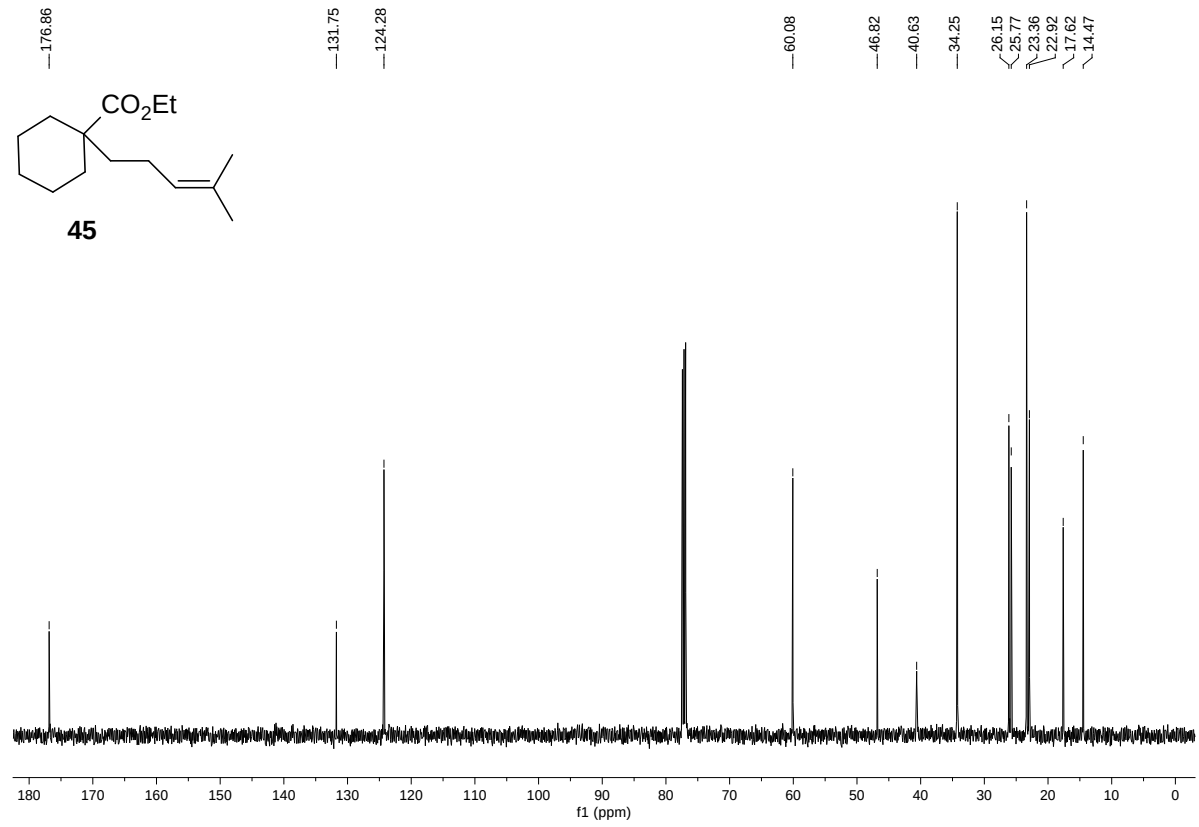
44


141.54
138.99
138.50
128.37
127.64
127.52
123.68
123.15
73.63
70.05
66.56
51.53
47.53
46.70
40.94
25.51
23.50
16.53
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

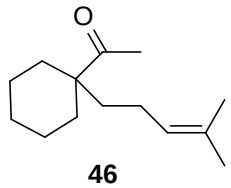

CO2Et

45

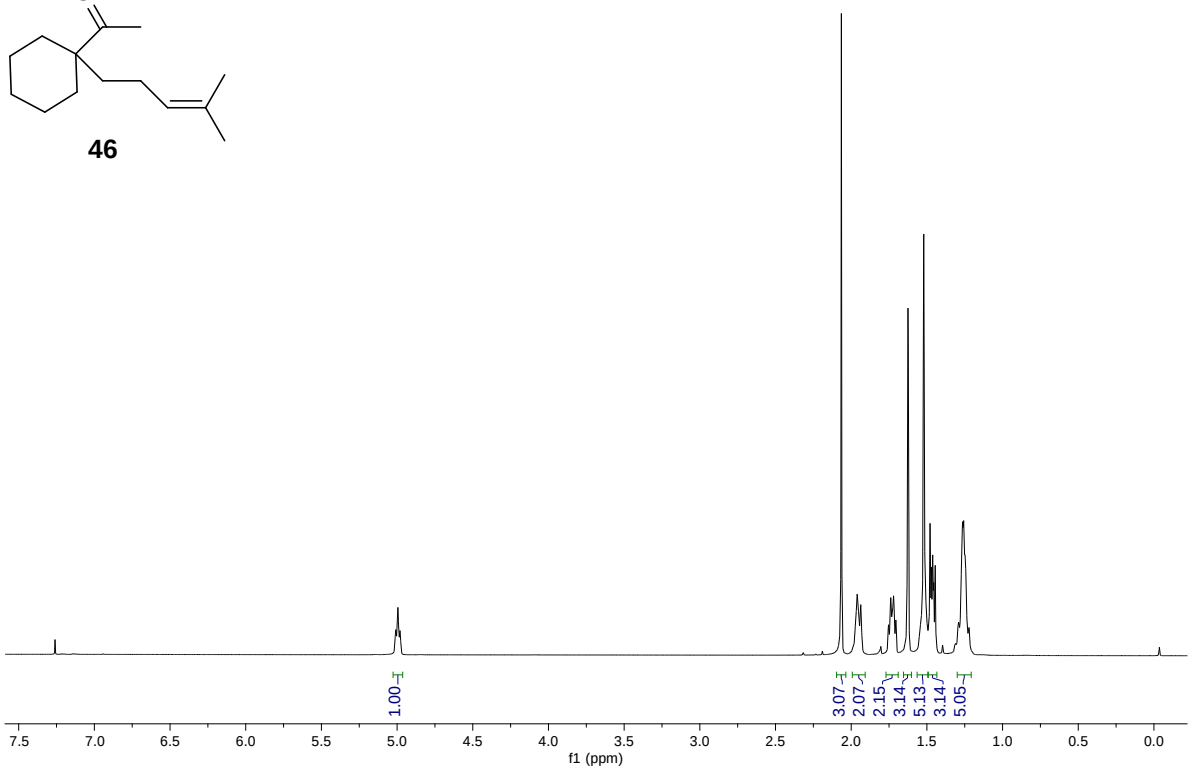

1.00
1.98
2.05
2.06
3.02
6.09
2.18
2.46
6.18
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


176.86
131.75
124.28
60.08
46.82
40.63
34.25
26.15
25.77
23.36
22.92
17.62
14.47
CO2Et
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

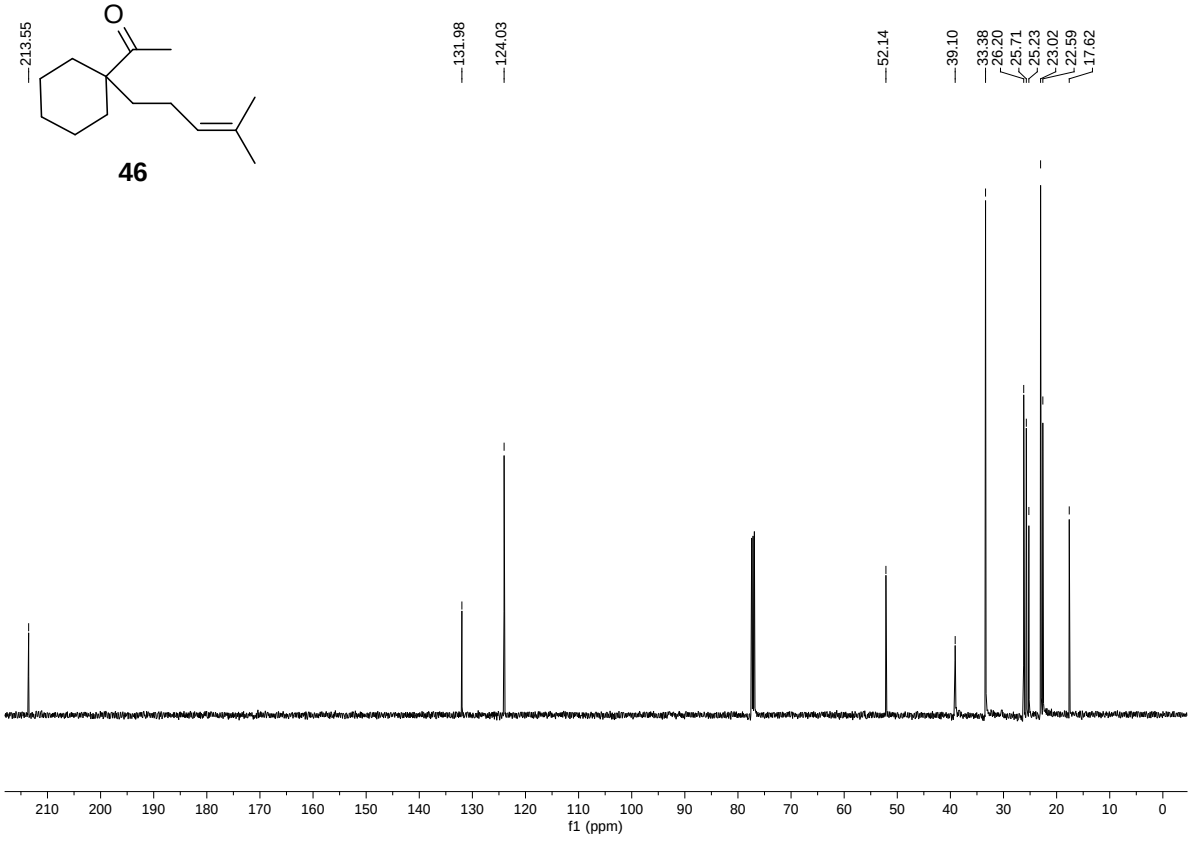
45

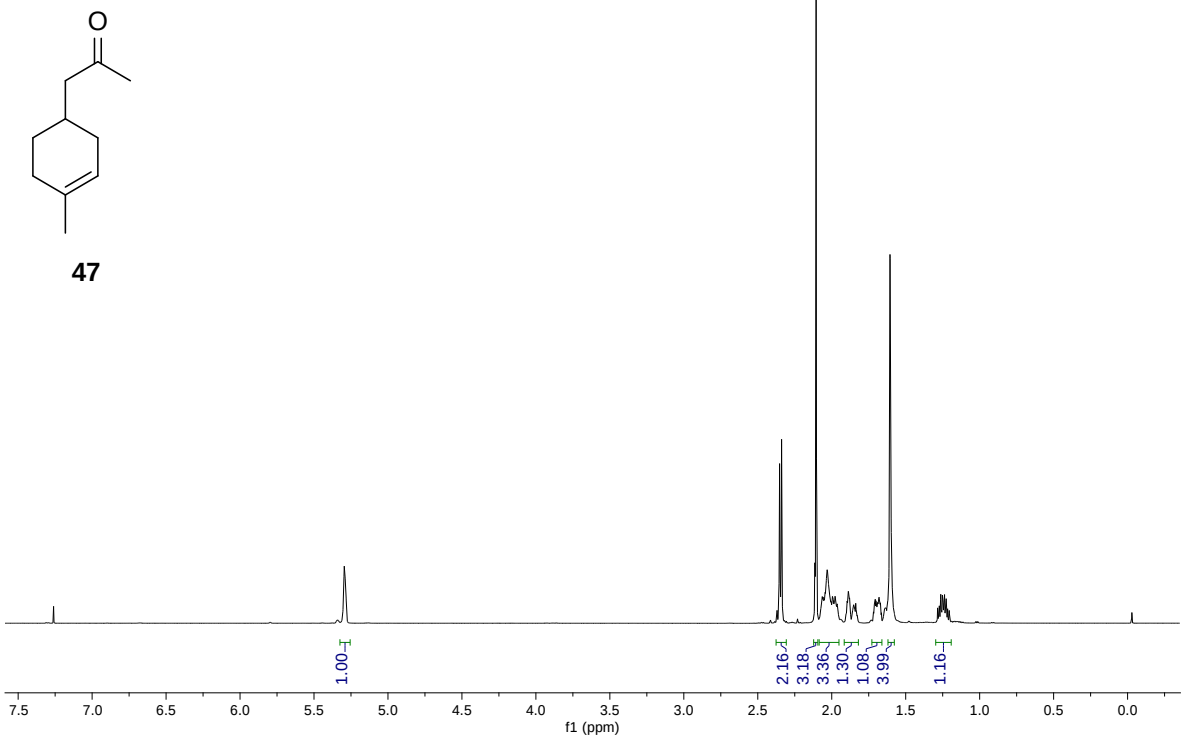


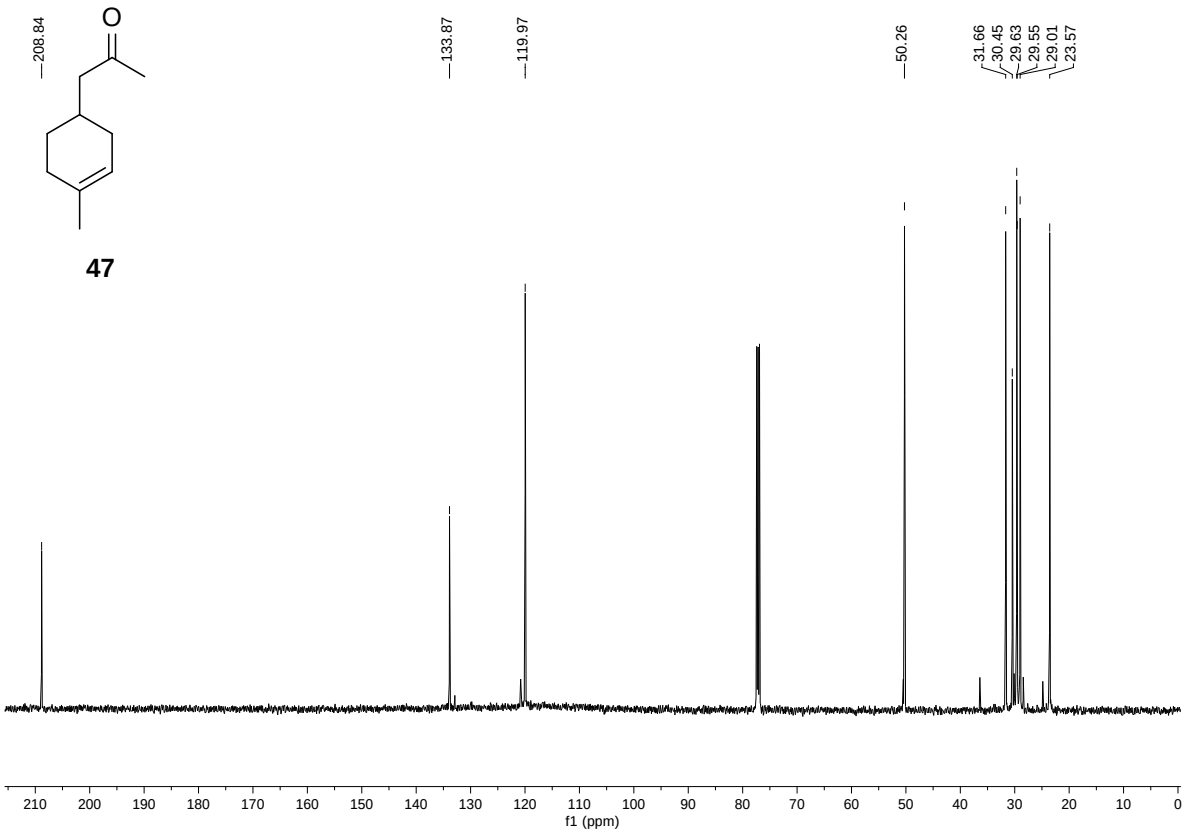
46


1.00
3.07
2.07
2.15
3.14
5.13
3.14
5.05
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

46

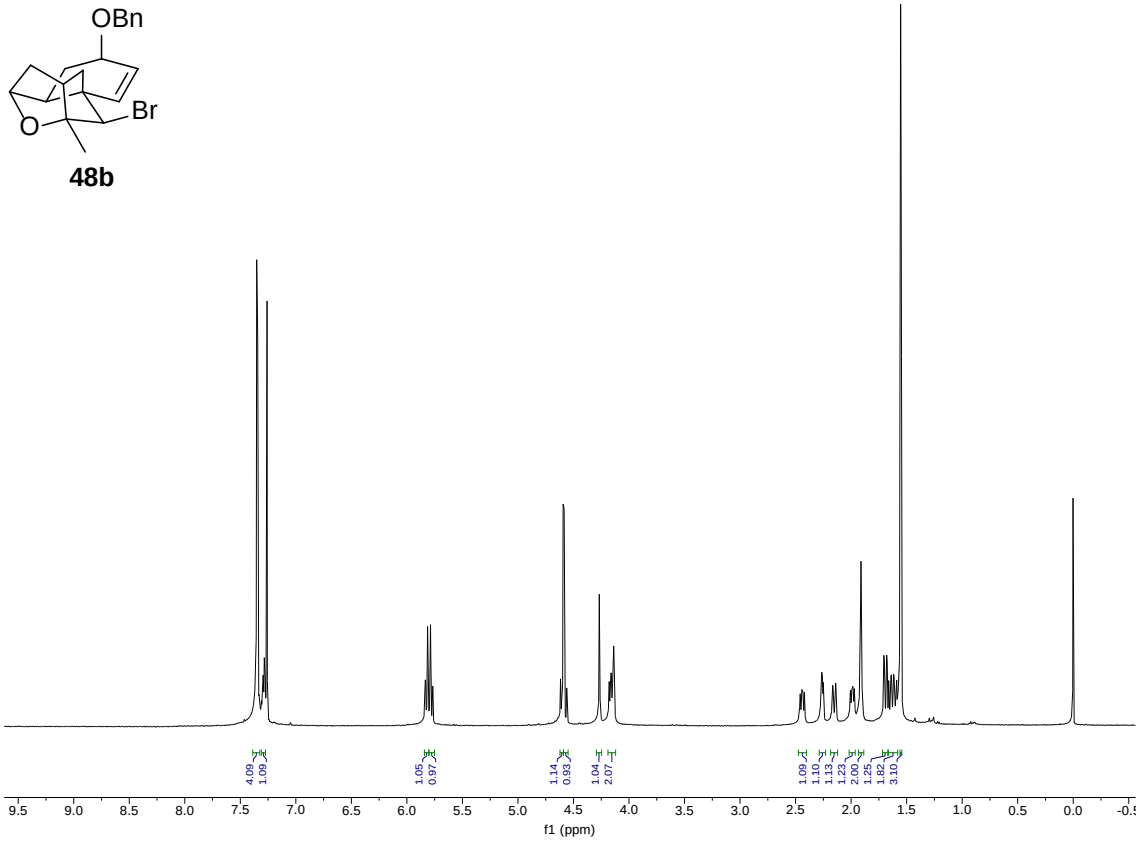

213.55
131.98
124.03
52.14
39.10
33.38
26.20
25.71
25.23
23.02
22.59
17.62
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

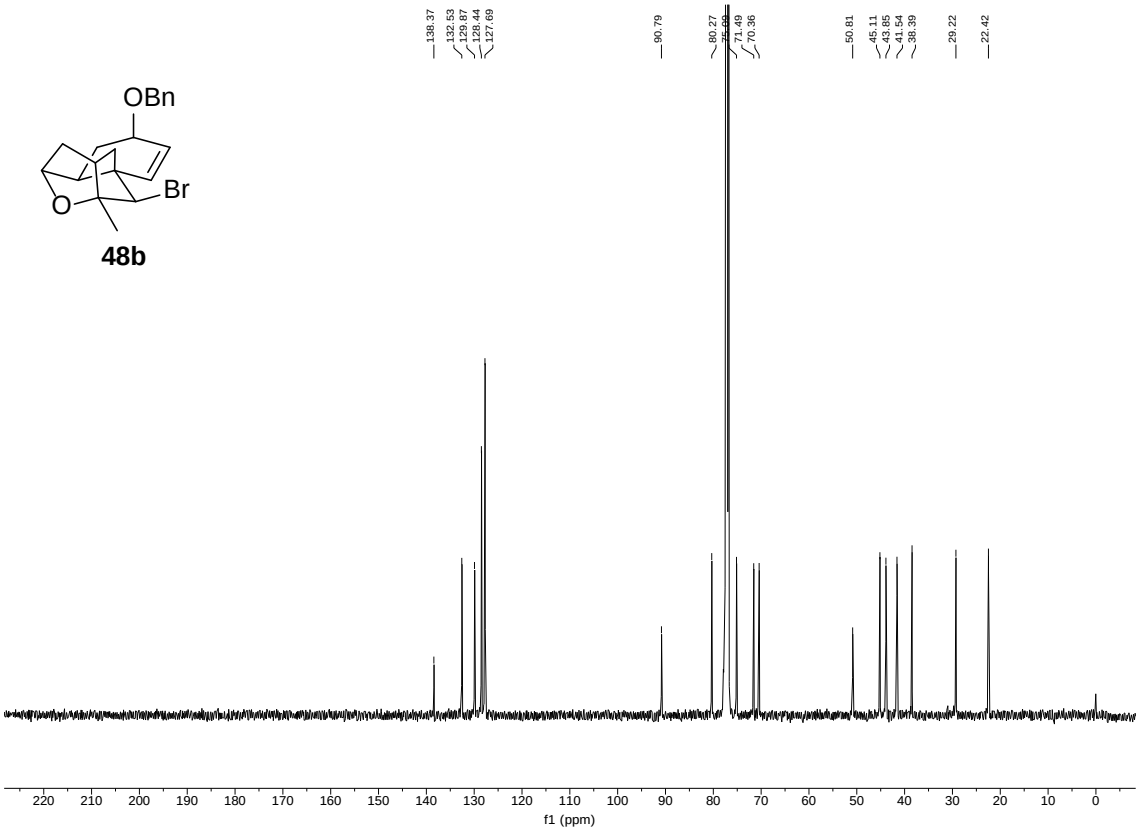

O
47
1.00
2.16
3.18
3.36
1.30
1.08
3.99
1.16
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


O
47
208.84
133.87
119.97
50.26
31.66
30.45
29.63
29.55
29.01
23.57
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

OBn
Br
O

48b


4.09
1.09
1.05
0.97
1.14
0.93
1.04
2.07
1.09
1.10
1.13
1.23
2.00
1.25
1.82
3.10
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


138.37
132.53
129.87
129.44
127.69
90.79
80.27
75.69
71.49
70.36
50.81
45.11
43.85
41.54
38.39
29.22
22.42
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

OBn
Br
O

48b

References

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